Pediatrics

VOLUME 3 MARCH 1949 NUMBER 3

## ORIGINAL ARTICLES

# MODE OF ACTION OF STREPTOMYCIN ON H. INFLUENZAE TYPE B. III. NATURE OF STREPTOMYCIN ACTION ON SENSITIVE H. INFLUENZAE

*By* HATTIE E. ALEXANDER, M.D., AND GRACE LEIDY, A.B.
*New York, N.Y.*

THE speed of the injurious effect of streptomycin on H. influenzae type B and the factors influencing it have gained fresh importance from the recognition that vestibular damage can follow only four to five days of streptomycin therapy.[1,2]

The limitations of streptomycin in treatment of influenzal meningitis have been caused mainly by the persistence of resistant cells; under these circumstances continuation of streptomycin therapy is useless. These resistant members, which have been shown to arise as the result of bacterial mutation,[3] have been found only in severe infections or, in other words, when the bacterial population in the spinal fluid is large.[4] Likewise in vitro, even though new resistant mutants are continuously arising, their rate of occurrence is so extremely low, averaging $10^{-11}$ per bacterium per bacterial generation, that their presence can be detected only when very large populations (over 100 billion) are examined. To eliminate such organisms, another antibacterial agent which operates through a different mechanism—for example, sulfonamides or type specific rabbit antiserum—must be used as an adjunct. Therefore, assessment of concentrations and exposure period of streptomycin needed in treatment of H. influenzae infections must relate to sensitive organisms.

This report presents data on the speed and character of the action of streptomycin on sensitive H. influenzae cells and the influence of the size of the population and concentration of streptomycin on the time required for this injurious effect. Experiments were designed for two purposes:

From the Babies Hospital and the Department of Pediatrics, Columbia University College of Physicians and Surgeons. Presented at the annual meeting of the Society for Pediatric Research. Atlantic City, N.J., May 4 and 5, 1948.

Work reported was supported by grants from the Commonwealth Fund.

(Received for publication September 16, 1948.)

1. To study the influence of size of bacterial population on the concentration of streptomycin needed to prevent growth of H. influenzae.
2. To determine the effect of size of bacterial population and concentration of streptomycin on the time required for lethal action on this organism.

## Materials and Methods

The three strains of H. influenzae used in these experiments were cultivated from spinal fluid of patients with meningitis before streptomycin therapy and were desiccated and sealed under vacuum of 5-10 microns of mercury (McLeod Gauge) within five days of isolation.[6] For each experiment to be reported a preserved culture was used to inoculate 3 ml. of Levinthal broth[3] in a tube.

I. Influence of size of bacterial population:

A. Examination of 1.5 to 2.0 billion organisms: The first broth culture of the preserved organisms was incubated 18 to 24 hours at 37.0° C. and then seeded in 0.5 ml. quantities on the surface of Levinthal agar in a petri dish. After incubation for six hours the luxuriant growth was removed with 5 ml. of broth and diluted to a density of approximately 120 on the Klett-Sommerson photoelectric colorimeter (green filter #54). This suspension diluted $10^{-1}$ through $10^{-7}$ for testing against lower concentrations of streptomycin,* 0.4 to 2.0 μg/ml., and undiluted for higher concentrations was seeded in 0.2 ml. quantities into pour plate preparations of Levinthal agar containing the following concentrations of streptomycin: 0.4, 0.8, 1.0, 1.2, 1.6, 2.0, 2.5, 3.5, 4.5, 5.5, 6.5 and 7.5 μg/ml.

Since these experiments deal with the action of streptomycin on the sensitive cells, 0.2 ml. samples of broth cultures have been considered representative of any similar sample of the same order of magnitude, up to a volume of 1 ml. To test this point 1.0 ml. samples were also used against 4.5 to 6.5 μg/ml. concentrations. There was no significant difference between the action of these concentrations when each pour plate preparation was seeded with a full 1 ml. and when 0.2 ml. quantities were used and the results multiplied by 5. This result was anticipated since the chances for this population to include a highly resistant mutant are remote; experimental data demonstrate one of these mutants in an average of 10 billion organisms. The results showing the effect of lower concentrations of streptomycin were also based on a fraction of the population and are calculated in all cases for 1 ml. by multiplying by the dilution factor. Calculations were based on results from the largest population of bacteria which permitted accurate counting of surviving colonies and which at the same time did not exert an inhibitory effect on colony formation because of the large size of the inoculum.

B. Examination of 5 to 12 thousand organisms per ml.: Levinthal broth seeded with a dried culture was incubated overnight; a subculture was incubated 6 to 10 hours when a 2 mm. loopful was seeded into 20 ml. of the same medium in a 125 ml. flask. After 14 to 16 hours' incubation the growth served as the culture for examination; the desired population size was arrived at by diluting this culture with broth to a density of approximately 60-70 on the Klett-Sommerson photoelectric colorimeter (green filter #54). With this suspension as a standard, a $10^{-4}$ dilution was used for seeding in 0.6 ml. quantities into each of six tubes of 5.4 ml. (final population 5,000 to 12,000/ml.) of Levinthal broth containing the following concentrations of streptomycin: 0.0, 0.8, 1.2, 1.6, 2.0 and 3.0 μg./ml. After 2, 4, 6 and 24 hours' incubation at 37.0° C., 0.5 ml. samples of each of these broth cultures in the varying concentrations of streptomycin, including the control with no streptomycin, were seeded into Levinthal agar pour plate preparations. Colony counts were recorded after 48 hours' incubation.

II. Factors influencing speed of lethal action:

Starting with the unadjusted broth culture as prepared under I B, corresponding to a population varying from 1.3 to 2.7 billion organisms per ml., dilutions $10^{-1}$ and $10^{-3}$ were made in Levinthal broth containing two different concentrations of streptomycin. These three different population sizes, approximately 1 to 2 billion, 100 to 200 million and 10 to 20 thousand/ml. were

* For experiments under I, A and B an early lot of relatively impure streptomycin sulfate was supplied by E. R. Squibb & Sons. For experiments under II a relatively pure streptomycin sulfate was supplied by Chas. E. Pfizer & Co.

exposed in 6 ml. volumes in tubes to two different concentrations of streptomycin, 10 μg. and 100 μg./ml., at 37.0° C. for varying lengths of time from 10 minutes to 24 hours. The number of organisms surviving under these varying circumstances was determined by seeding at the various time intervals 0.5 ml. samples into pour plate preparations of Levinthal agar; after 48 hours'

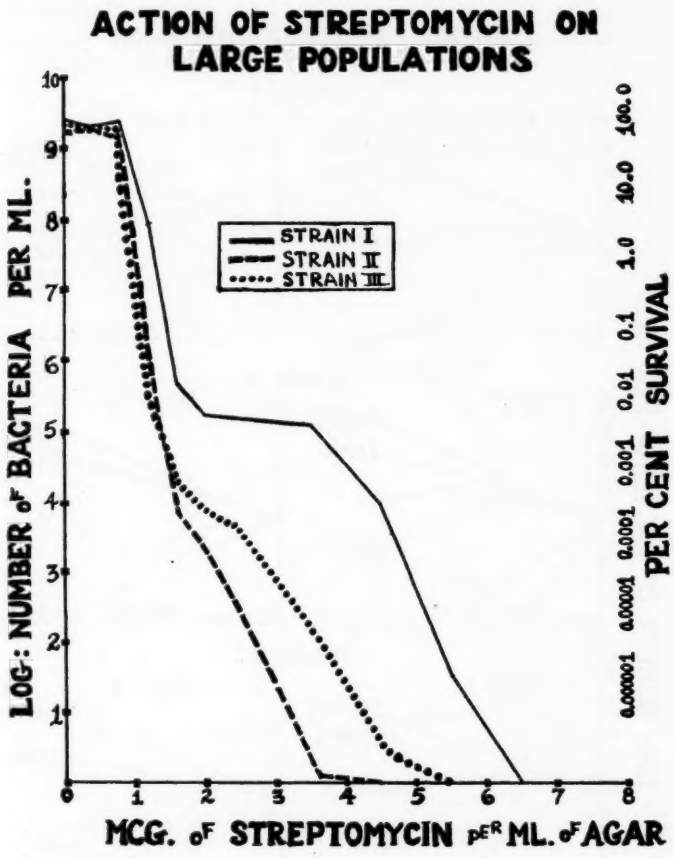
ACTION OF STREPTOMYCIN ON LARGE POPULATIONS
LOG: NUMBER OF BACTERIA PER ML.
PER CENT SURVIVAL
STRAIN I
STRAIN II
STRAIN III
MCG. OF STREPTOMYCIN PER ML. OF AGAR

FIG. 1

incubation the colony counts were recorded. When suspensions of organisms contained concentrations of streptomycin believed to be sufficient to inhibit growth when seeded in the pour plate preparation, two appropriate measures were taken to remove this effect: for samples cultured after 10 and 30 minutes' incubation, simple dilution was used; specimens which had been exposed to streptomycin during incubation for one hour or more were centrifuged and resuspended in broth before being mixed with agar for pouring. The concentrations of streptomycin in spinal fluid were determined by the broth dilution method of Donovick et al.[6]

## EXPERIMENTAL RESULTS

I. To determine the influence of size of population on the concentration of streptomycin needed to prevent growth two different population sizes were studied: approxi-

mately 10 thousand and 1.5 to 2 billion organisms/ml. This choice was guided by three reasons: the range of variation is comparable to the population densities found in spinal fluid of patients with meningitis; the two levels chosen can be expected to bring out effects due to numbers; and confusion of results by the presence of highly resistant

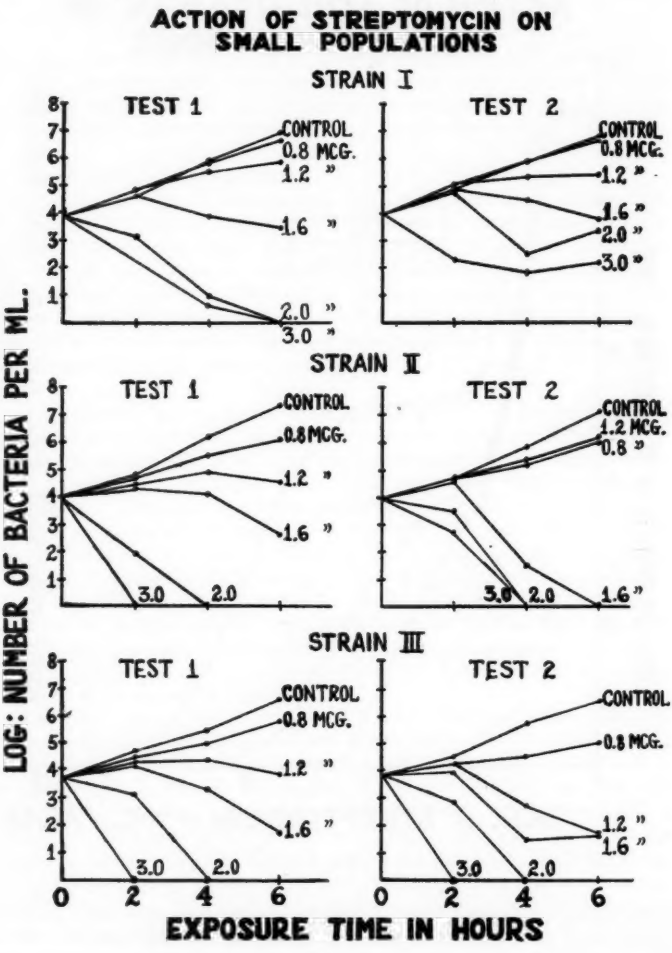


FIG. 2

mutants, normally present in very large populations, is unlikely. The concentrations of streptomycin required to prevent the growth of 1.5 to 2 billion organisms of three different strains when seeded in pour plate preparations of Levinthal agar are shown in Fig. 1. The number of organisms in logs is plotted on the ordinate and the concentration of streptomycin on the abscissa. A rough estimate of the percent of organisms surviving at each concentration of streptomycin is shown on the right parallel with the ordinate. The curve representing each strain is the average obtained from three experi-

ments. One to 1.2 μg./ml., the lowest concentrations which prevent growth of a significant proportion of the population of these three strains, actually eliminate 90% of the cells. A very small increase, to 1.6 μg./ml., prevents the growth of 99.99% of all organisms. To eliminate the remaining very small fraction concentrations of 4.5 to 6.5 μg./ml. are required.

The minimal concentrations of streptomycin which prevent the growth of small populations, 5 to 12 thousand organisms/ml., are presented in duplicate for three different

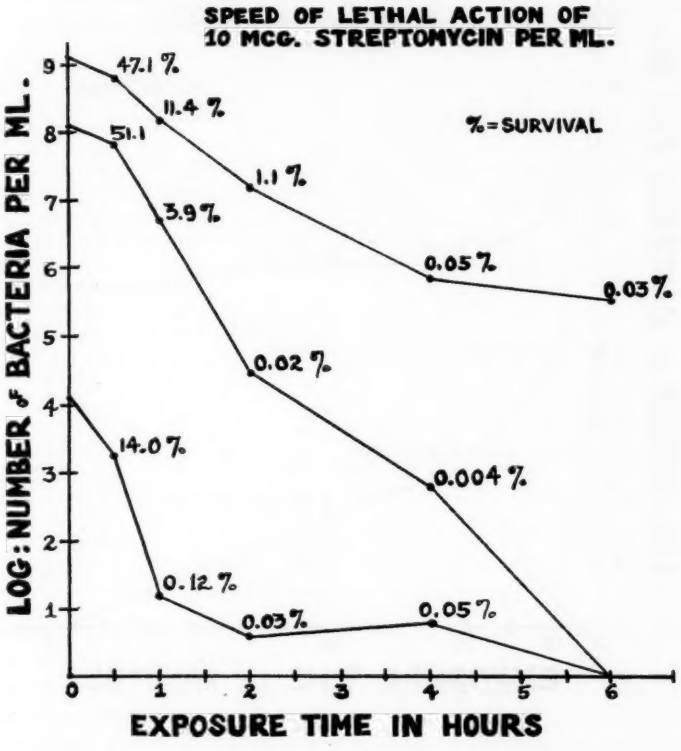


FIG. 3

strains in Fig. 2. The exposure time necessary for lethal injury is also shown. The number of viable organisms/ml. is plotted in logs on the ordinates and the duration of exposure to streptomycin at the time of sampling in hours on the abscissa. The influence of each concentration of streptomycin studied is shown by a curve connecting the points representing the number of viable organisms present after two, four and six hours; the 24 hours reading is not included. It is seen that while the control increases from approximately 10 thousand to 10 million organisms/ml., within six hours exposure to a concentration of 2 to 3 μg./ml. with one exception not only prevents growth but is apparently lethal; viable organisms are not demonstrable after exposure for six hours. In test 1 of strain 1, concentrations of 2 and 3 μg./ml. were lethal at six hours. In the other test of strain 1, even 3 μg./ml. failed to sterilize the culture in six hours;

this point was reached some time between six and 24 hours. It is also evident that a portion of the population is killed by concentrations lower than 2 μg./ml. With strains 2 and 3, a concentration of 2 to 3 μg./ml. prevents growth within two to four hours.

From the results of examination of these two populations—approximately 10 thousand, and 1.5 to 2 billion organisms per ml.—certain facts are apparent:

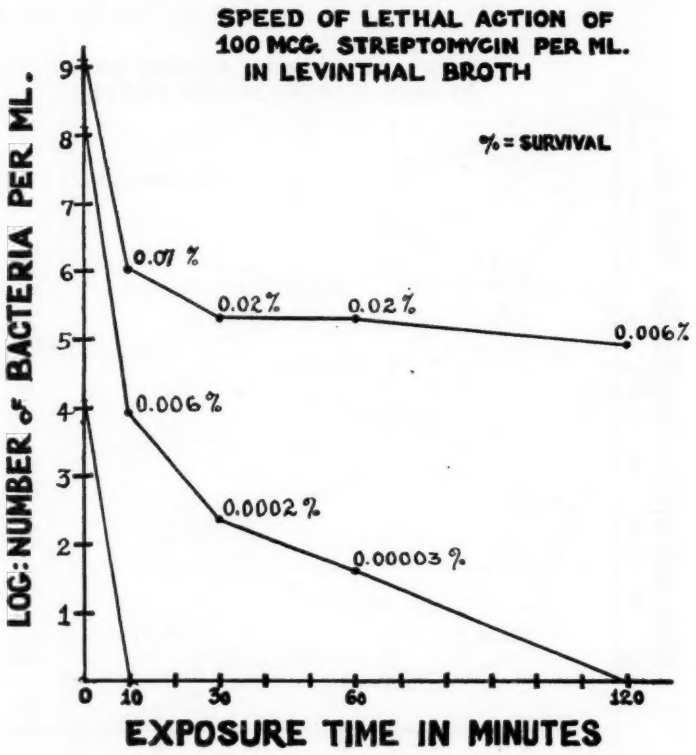


FIG. 4

1. There is a lack of uniformity of susceptibility among members of both populations.

2. While consistent elimination of 100% of the smaller population required 2-3 μg./ml., and for the larger population 4.5 to 6.5 μg./ml., 1.6 μg./ml. killed 99% of both small and large populations of two of the three strains.

II. The influence of population size and concentration of streptomycin on the speed of lethal action is shown by the results of exposing three different population sizes to two concentrations of streptomycin, 10 μg. and 100 μg./ml.

The effect of 10 μg. of streptomycin per ml. on three different populations, 1.3 billion, 130 million and 13 thousand is shown in Fig. 3. This concentration is lethal for the small population within six hours; only 0.1% remains at one hour. A population of 130 million is reduced to 0.02% within two hours and all cells are killed at six hours.

While 98% of the 1.3 billion population is eliminated after a two hour period, complete elimination of the population is not accomplished in 30 hours; the survivors were not resistant to 10 μg./ml. By contrast, a concentration of 100 μg. streptomycin per ml., as is apparent from Fig. 4, exerts a more rapid lethal effect on all three populations. Exposure to 100 μg./ml. for 10 minutes eliminates 100% of the 13 thousand population, 99.99% of the 130 million and 99.93% of the 1.3 billion. The 130 million popula-

TABLE I

SPEED OF LETHAL ACTION OF STREPTOMYCIN—VIABLE BACTERIA PER ML. AFTER PERIODS OF EXPOSURE INDICATED

| μg. per ml. | Before | 10 min. | 30 min. | 1 hr. | 2 hr. | 4 hr. | 6 hr. | 24 hr. |
|---|---|---|---|---|---|---|---|---|
| | 2,360,000,000 | 60,000 | 21,800 | 2,060 | 7 | 0 | 0 | |
| | 2,060,000,000 | | 368,000 | 56,000 | 25 | 0 | 0 | |
| | 1,300,000,000 | 958,000 | 216,000 | 204,000 | 85,200 | 1,760 | 5,200 | 0 |
| 100 | 195,000,000 | 130,000 | | 0 | 0 | | | |
| | 172,000,000 | 16,000 | 20 | 0 | 0 | | | |
| | 130,000,000 | 8,180 | 230 | 40 | 0 | 0 | 0 | |
| | 17,000 | 0 | | | | | | |
| | 13,000 | 0 | | | | | | |
| | 187,000,000 | | 144,000,000 | 1,800,000 | 106,000 | 53,600 | 3,000 | 0 |
| | 130,000,000 | | 66,400,000 | 5,100,000 | 28,400 | 590 | 0 | 0 |
| 10 | 18,700 | | 8,300 | 22 | 0 | 0 | 0 | |
| | 27,800 | | 8,440 | 42 | 0 | 0 | 0 | |
| | 13,000 | | 1,820 | 16 | 4 | 6 | 0 | |

tion is destroyed after two hours but this point is not reached for the 1.3 billion until some time between six and 30 hours.

The results of other experiments in which comparable populations were exposed to these two concentrations of streptomycin for varying periods are listed in Table I. The cause of variations seen occasionally with populations of the same size and with a comparable exposure to the same streptomycin concentration has not been explored.

## DISCUSSION

The results of these experiments raise two questions which have an important bearing on clinical therapy: 1. What population sizes are found in the spinal fluid of patients with influenzal meningitis, and 2. What concentrations of streptomycin are maintained in the spinal fluid after intrathecal administration of 25 mg., an accepted therapeutic dose? Table II presents data bearing on the first question. Spinal fluids from 11 different patients prior to treatment were seeded in measured quantities into pour plate preparations of Levinthal agar and colony counts were made after 48 hours' incubation. The results are listed on the basis of the number of colonies per ml. of spinal fluid; to

obtain the total population of viable organisms these figures must be multiplied by approximately 100. The concentrations of sugar in these spinal fluids are also tabulated. With one exception there appears to be a negative correlation between the concentration of spinal fluid sugar and the size of the bacterial population; the greater the number of organisms, the lower the sugar concentration.

Data referring to the second question are shown in Table III. After introduction of 25 mg. of streptomycin intrathecally the concentration in the spinal fluid* was measured

TABLE II

CORRELATION BETWEEN CONCENTRATION OF SUGAR AND SIZE OF BACTERIAL POPULATION IN 11 PATIENTS

| Patient | Spinal Fluid Sugar Concentration mg.% Before Treatment | Viable Organisms per ml. of Initial Spinal Fluid |
|---|---|---|
| 1 | 5 | 334,000,000 |
| 2 | 9 | 356,000,000 |
| 3 | 11 | 24,000,000 |
| 4 | 18 | 72,000 |
| 5 | 23 | 660 |
| 6 | 24 | 17,000 |
| 7 | 24 | 6,000 |
| 8 | 27 | 4,000,000 |
| 9 | 29 | 8,340 |
| 10 | 29 | 20 |
| 11 | 44 | 1,830 |

TABLE III

CONCENTRATION OF STREPTOMYCIN IN SPINAL FLUIDS OF PATIENTS RECEIVING 25 MG. INTRATHECALLY

| Time after administration | Patient I | Patient II |
|---|---|---|
| | Streptomycin μg./ml. | Streptomycin μg./ml. |
| ½ hour | 410 | |
| 1 hour | 368 | 204 |
| 2 hours | 74 | 149 |
| 3 hours | 104 | |
| 24 hours | 6 | 7 |

at ½, 1, 2, 3 and 24 hours in two patients. It is apparent that the concentrations which are required in vitro to exert rapid lethal action even on large populations are maintained for at least three hours.

Demonstration of the rapid in vitro bactericidal action of streptomycin on H. influenzae, together with the sterilization of spinal fluid within 24 hours after streptomycin administration in most patients, suggest that a 24-hour period of streptomycin therapy, 40 mg./kg. intramuscularly and one intrathecal dose of 25 mg., will be adequate for elimination of all sensitive organisms. The addition of sulfadiazine, which acts through a different mechanism, can be expected to eradicate the very small fraction of bacterial

* Concentrations measured at the Squibb Institute for Medical Research.

cells which for unexplained reasons may persist, as well as the highly resistant mutants which may be present when the total population is very large.

## Summary

Data presented demonstrate that members of H. influenzae type B populations are not uniformly sensitive to streptomycin. Over 99% are susceptible to 1.6 μg./ml.; the larger the population, the wider the variation in resistance of the small fraction surviving.

The injurious action of streptomycin on H. influenzae type B is primarily bactericidal.

Streptomycin in concentrations between 10 and 100 μg./ml. exerts a rapid lethal action; the greater the concentration of the antibiotic, the greater the speed. Significant increases in population size increase the time required for bactericidal action.

The data presented suggest that when streptomycin is used in the treatment of H. influenzae infections in man, its intramuscular administration over a period not longer than 24 hours will ordinarily suffice to obtain a maximal streptomycin effect; that in cases of meningitis the addition of a single intrathecal dose of streptomycin of 25 mg. will be adequate; and that the use of sulfadiazine as an adjuvant is advisable to bring under control the eventual resistant mutants which may survive the bactericidal action of streptomycin.

## References

1. Alexander, Hattie E., Leidy, Grace, Rake, G., and Donovick, R., Hemophilus influenzae meningitis treated with streptomycin, J.A.M.A. **132**:434, 1946.
2. Alexander, Hattie E., and Leidy, Grace, Present status of treatment for influenzal meningitis, Am. J. Med. **2**:457, 1947.
3. Alexander, Hattie E., and Leidy, Grace, Mode of action of streptomycin on type b H. influenzae; nature of resistant variants, J. Exper. Med. **85**:607, 1947.
4. Alexander, Hattie E., and Leidy, Grace, Mode of action of streptomycin on type b H. influenzae; origin of resistant organisms, J. Exper. Med. **85**:329, 1947.
5. Brown, J. H., Vacuum tubes for storage and shipment of bacteria, Science **44**:429, 1926. (Also personal communication.)
6. Donovick, R., Hamre, D., Kavanagh, F., and Rake, G., Broth dilution method of assaying streptothricin and streptomycin, J. Bact. **50**:623, 1945.

## Spanish Abstract

### Modo de Acción de la Estreptomicina en H. Influenzae Tipo B. III. Naturaleza de la Acción de la Estreptomicina en H. Influenzae Sensitivas

Los datos presentados demuestran que miembros de población H. influenzae tipo B. no son uniformemente senstivos a la estreptomicina. Más del 99% son susceptibles a 1.6 μg./ml. Entre mayor sea la población, más será la variedad en resistencia de la pequeña fracción que sobrevive.

La acción perjudicial de la estreptomicina en H. influenzae tipo B. es primariamente bactericida.

La estreptomicina en concentraciones entre 10 y 100 μg./ml. ejerce una acción letal rápida; entre mayor sea la concentracion del antibiótico, mayor será la velocidad. Aumentos significativos en el tamaño de la población alargan el tiempo requerido para la acción bactericida.

Los datos presentados sugieren que cuando se usa la estreptomicina en el tratamiento de infecciones de H. influenzae en el hombre, su administración intramuscular por un período de no más de 24 horas será ordinariamente suficiente para obtener un efecto máximo de estreptomicina; que en casos de meningitis la adición de una simple dosis intratecal de estreptomicina de 25 mg. será adecuada, y que se recomienda el uso de sulfadiazina como un adyuvante para controlar mutantes resistentes que puedan sobrevivir la acción bactericida de la estreptocimina.

*622 W. 168th St.*

# CONGENITAL CHONDROSTERNAL PROMINENCE (PIGEON BREAST) A NEW INTERPRETATION

*By* HENRY A. BRODKIN, M.D.
*Newark, N.J.*

TEXTBOOKS of pediatrics[1] describe a "prominence of the sternum and the cartilaginous parts of the ribs, with a depression of the sides of the thorax" under such names as pigeon breast, chicken breast, pectus carinatum, keel-shaped breast and piriform chest. The name congenital chondrosternal prominence is suggested for this deformity; because, first, it adequately describes the deformity instead of comparing it to the shape of the breast of a fowl from which it differs anatomically, or a pear, or a keel of a ship, etc.; second, it refers to its congenital origin; and, third, it is more readily coordinated with its opposite deformity which the author has chosen to call congenital chondrosternal depression[2] (funnel chest).

The author has stated, in a previous article,[2] reasons for suggesting the term congenital

FIG. 1. Mongoloid, Negro infant, 14 mo. old with well developed congenital chondrosternal prominence (pigeon breast). Upper thorax is round and lower thorax is elliptical and retracted.

chondrosternal depression. The same situation applies to congenital chondrosternal prominence. Therefore, it is suggested that appropriate terms for the deformities of the sternum and its adjacent cartilages should be 1. congenital chondrosternal depression (funnel breast) and 2. congenital chondrosternal prominence (pigeon breast).

## ETIOLOGY

Just as congenital chondrosternal depression has been attributed to various conditions, such as rickets, respiratory obstructive lesions and intrauterine compressive forces, so also

(Received for publication August 4, 1948.)

has the etiology of congenital chondrosternal prominence been variously described. Griffith-Mitchell[3] state, "it is a symptom of rickets but it also occurs in prolonged interference with respiration such as from the presence of adenoids." Marques[4] attributes the deformity to a combination of factors resulting from severe prolonged dyspnea or cough in cardiorespiratory affections. He states that the deformity was due to the severe dyspnea in a case of tetralogy of Fallot. Eichhorst[5] regards the "thorax of the pigeon" as a rachitic thorax. Schiassi[6] in describing "the piriform thorax of Wenckebach" quotes Wenckebach as stating that the deformity is the result of a low and atonic diaphragm resulting from visceroptosis. DeCastro[7] and Romeiro[8] in discussing varieties of thoraces believe that each is dependent on the type of dyspnea or respiration. Horder and Gow[9] ascribe chest deformities to obstructive lesions of the airways occurring in infants.

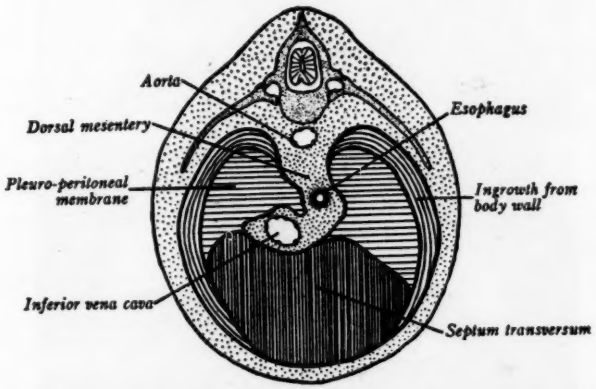


FIG. 2. (From Arey's Developmental Anatomy) 1. Septum Transversum which becomes the anterior portion. 2. Oleuro-peritoneal membrane which forms the lateral portion. 3. Dorsal mesentary which forms the posterior portion. 4. Muscular ingrowth from body wall which contributes to the circumferential muscular portion.

Mitchell and Nelson[1] deal very briefly with the subject and do not discuss the etiology. Holt and McIntosh[10] only raise a doubt that the deformity "depends on rickets alone." In speaking of congenital deformities of the chest they mention "funnel chest and pigeon breast." Brenneman[11] classifies this deformity in the acquired group and states it is a manifestation of rickets. Graham, Singer and Ballon[12] state, "Rickets, enlarged adenoids and tonsils, and tuberculous spine disease are said to be responsible for the condition."

In a survey of 41,863 school children in the Newark school system,[13] 25 children were found with this deformity, an incidence of .06%. This survey indicates: 1. low incidence of the condition, 2. it does not interfere with normal activity and 3. there is no relationship to obstruction of the air passages which is a common finding. Blalock[14] states that while chest deformities are not uncommon among patients with congenital heart disease, the vast majority have normal thoraces. One may assume therefore that dyspnea and respiratory obstructions are not etiologic factors in the production of this deformity. Furthermore the deformity usually begins to manifest itself shortly after birth and progresses as the child grows older.

A closer study of the action of the diaphragm indicates that a variation from the

normal structure will produce an unequal pull on the anterior region of the thorax. The posterior portion of the diaphragm is the anchor point and is firmly attached to the lumbar vertebrae and twelfth rib. This attachment is unyielding. Examination of the diaphragm of the case reported shows the anterior portion of the diaphragm as a comparatively thin tendinous attachment to the more movable edge of the lower anterior thoracic wall. A greater pull in this area will produce a change in its contour. This is the area where most chest deformities occur. Examinations of complete diaphragms in all ages of normal thoraces indicates a fairly uniform structure with a normal relationship between the circumferential muscular membrane and the central trefoil shape tendinous

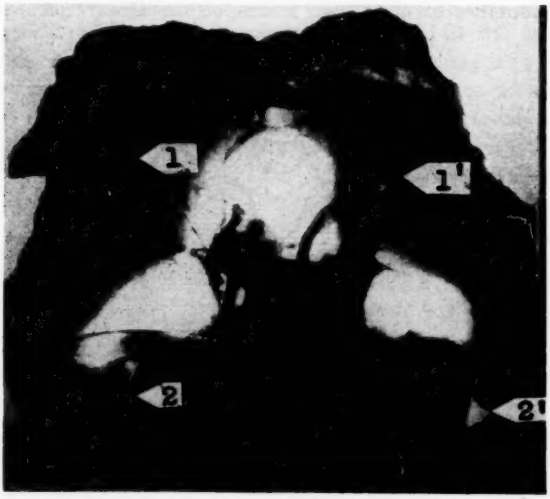


FIG. 3. Normal diaphragm from a normal chest with typical trefoil or clover leaf central tendinous portion. 1 and 1′ indicate raphe separating anterior from lateral portions. 2 and 2′ indicate vertebrocostal trigone separating the posterior from the lateral portions. Note the uniform muscular development.

membrane. (See Fig. 3 Normal Diaphragm.) Observations and experience with congenital chondrosternal depression, and the opportunity to study a case of congenital chondrosternal prominence, led me to conclude that the underlying etiology is some congenital developmental alteration in the structure of the diaphragm. A study of the embryologic development of the diaphragm reveals the numerous opportunities for the occurrence of variations from the normal structure.

## DEVELOPMENT OF THE DIAPHRAGM

According to Arey,[15] the diaphragm is derived from four sources: "1. its ventral portion from the septum transversum; 2. its lateral part from the pleuroperitoneal membranes, plus 3. derivatives from the body walls; 4. and last, a median dorsal portion is contributed by the dorsal mesentery. In addition to these components there is the striated muscle of the diaphragm which traces origin to a pair of pre-muscle masses lying opposite the fifth cervical segments of 9 mm. embryos. . . . The muscle masses migrate

caudally with the septum transversum and develop chiefly in the periphery of the diaphragm." Ultimately a fusion of these component segments occurs. Some of the muscle fibers degenerate to form tendinous fibers which make up the trefoil central tendon. The normal diaphragm therefore consists of a peripheral muscular membrane with muscle fibers radiating centrally into the central tendinous membrane which is trefoil in shape and incompletely divided into three lobes or leaflets (Fig. 3).

The muscular portion of the diaphragm following its embryologic derivations is divided into four portions. The anterior portion arises behind the gladiolar-xiphoid junction of the sternum and the lower cartilaginous margin of the anterior chest wall and is inserted into the anterior leaf of the trefoil tendinous membrane. This anterior portion is often further divided into two sternal parts separated by a median raphe. Just lateral to the narrow sternal parts there often is a raphe which divides the sternal parts from the remainder of the anterior portions. The two lateral portions of the diaphragm arise on the inner surfaces of the lower ribs and are inserted into the outer margin of the two lateral leaves of the trefoil membrane. The posterior portion arises from the upper lumbar vertebrae and twelfth rib and is inserted into the posterior margin of the anterior leaf and the posterior and medial margins of the lateral leaves of the trefoil membrane. A distinct raphe separates the anterior portion from the lateral portions. (See 1 and $1^1$ in Fig. 3). The vertebro-costal trigones which are tendinous and devoid of muscle fibers separate the posterior portion from the lateral portions (See 2 and $2^1$ in Fig. 3). The contraction of this normal type of diaphragm aids in the normal development of the thorax beginning with the first inspiration.

## Physiologic Considerations

At birth, the transverse and antero-posterior diameters of the chest are practically equal. In the early months of infancy, the contraction of the diaphragm is the chief mechanism of respiration.[16] In the first year of life, it is the greatest factor in converting the infantile round chest into the normal elliptical shape. The vertical axis increases more rapidly in length so that the shape of the thorax becomes conical. This mechanism also produces changes in the ribs by causing them to slant downward and thus affect their leverage with the vertebrae. The ribs grow out laterally and the sternum is moved downward. All other factors being equal, only a normally developed and functioning diaphragm will cause these physiologic changes which produce a normally shaped thorax.

Functionally, the contraction of the posterior portion of the diaphragm, which is anchored to the immobile lumbar vertebrae and twelfth rib, acts solely to increase the vertical diameter of the thorax. Contraction of the costosternal portion of the diaphragm moves it downward and forward. This action pushes the abdominal viscera forward and then raises the lower anterior ribs to which this portion of the diaphragm is attached.[15] It also tends to force the sternum forward and upward. The function of this action is to increase the antero-posterior and lateral diameters of the thorax. The type of respiration of normal infants is largely "abdominal."

In congenital chondrosternal prominence, the diaphragmatic musculature differs from the normal in that the anterior or chondrosternal portion is tendinous and contains few muscle fibers and the musculature of the lateral and posterior portions is thick and strong. The normal mechanism is altered so that the anterior lower ribs instead of being elevated and raised are retracted on inspiration. At the same time, instead of the abdominal viscera's being pushed forward the epigastrium is retracted. In this deformity the upper

portion of the anterior thorax remains round and "infantile" instead of becoming elliptical. Such an infant must rely entirely on the vertical enlargement of the thorax by the contraction of the posterior half of the diaphragm for inspiration. Not only is there no enlargement in the antero-posterior and lateral diameters of the thorax but there is actually diminution during inspiration. This paradoxical action produces the apparent labored respiration which is seen in this deformity. The following case report will illustrate these facts.

## Case Report

R. S., Negro female, 14 months old, was admitted to Newark Beth Israel Hospital for treatment of a "cold." For the previous two days, the infant had had a severe cough productive of mucopurulent sputum and a temperature of 37.8°C.

*Past History:* The infant was born normally almost at full term. She developed slowly and had pneumonia at four months of age. She made an uneventful recovery from this. The mother first noted the chest deformity at this time and stated that it had been increasing in size since. The infant did not learn to stand or walk.

*Physical Examination:* Well nourished but under-developed infant, 76 cm. long, weighing 6.5 kg. The head measures 42 cm. in circumference and the chest 43 cm. She could sit up but did not crawl. Both fontanelles wide open. The face had mongoloid features. There were no teeth. The neck was short. The chest had the typical protrusion of the upper portion of the sternum and the adjoining costal cartilages. Laterally, the chest appeared narrowed and had deep Harrison's grooves on each side. The lower antero-lateral ribs flared out and the lower portion of the sternum and xiphoid process were depressed. Respiration appeared labored and abnormal. During inspiration, the protruding portion appeared to be immobile, but the costal margins were elevated and the lower descending portion of the sternum and adjoining epigastrium were retracted. This paradoxical action appeared to force the anterior portions of the expanding lungs against the bow of the anterior chest wall. On expiration, the costal margins descended and the parts of the chest and abdomen that were retracted by the pull of the diaphragm during inspiration returned to their previous positions. The lower extremities were kept in a "frog-leg" position with thighs superabducted. The lungs were negative except for moist rales throughout. In the heart examination, a thrill was felt and a marked, continuous, systolic murmur was heard most strongly over the third left intercostal space. The remainder of the examination was not pertinent.

*Laboratory Reports:* The blood and urine studies were all normal. Tuberculin test was negative. Blood chemical studies revealed serum calcium 10.3 mg./100 cc., phosphorus 3.4mg./100 cc., alkaline phosphatase 3.6 Bodansky units, cholesterol 231 mg./100 cc., serum albumen 3.7 gm. and serum globulin 2.5 gm. The pediatric service concluded that there was no rickets present and the diagnosis was mongolism, congenital heart disease, pigeon breast and upper respiratory infection.

The X-ray report indicated only a mitral shaped heart, enlarged in all its chambers suggesting an underlying congenital cardiac lesion. It appeared that the deformity was aggravated during the inspiratory phase of respiration, coincident with the contraction of the diaphragm. The obvious question arose: were the diaphragmatic contractions responsible for the chest deformity? Fluoroscopy disclosed that both leaves of the diaphragm were of normal contour, and excursions were equal and normal. Crying increased the diaphragmatic motion equally.

To eliminate the action of the diaphragm as the responsible factor, the left phrenic nerve was injected above the clavicle with 3 cc. of 1% novocain solution. In a few minutes, the effect was obvious. The inspiratory retractions on the left side ceased but continued on the right side. The left costal margin moved normally. Fluoroscopy demonstrated that the left leaf of the diaphragm was paralyzed. Three days later, in order to have a permanent record of the effect of this test, motion pictures were taken before and after the right phrenic nerve was injected in a similar manner. The same effect was observed. Pictures were taken of a normal child of approximately the same age to observe the contrast.

As a result of these tests and observations, it was concluded that this deformity is a result of a malformation of the structure of the diaphragm which produced this peculiar retraction during inspiration. Brown's procedure of severing the diaphragmatic anterior attachment at the gladiolar-

xiphoid junction had proved effective in preventing the further development of congenital chondrosternal depression in infants. Consideration was therefore given to a surgical procedure which would disrupt the abnormal influence of the diaphragm in this infant and prevent the further progression of this deformity. Such a surgical procedure would of necessity have to be simple and devoid of danger inasmuch as the deformity is only unsightly and does not produce cardiorespiratory

FIG. 4. Abnormal diaphragm with congenital chondrosternal prominence (pigeon chest). Note inverted V shape of tendinous portion. Poor muscular development of the anterior portion and absence of muscle fibers in the sternal portion. Raphe 1, 1′ separating anterior and lateral portions. Strong muscular development of lateral and posterior portions and absence of tendinous vertebrocostal trigones.

symptoms as is sometimes the case with the chondrosternal depression. Furthermore, the abnormal anatomic changes of the diaphragm in this deformity had never been correlated thus far. However, the infant developed a severe bronchitis and died suddenly, six weeks after admission.

### AUTOPSY FINDINGS

The fontanelles were widely separated. The thymus gland was enlarged. Fetal lobulations were present in the left lung. The heart chambers were enlarged and the musculature hypertrophied.

There was a large interventricular septal defect. The pulmonary vessels were dilated. The anterior chest wall, on removal, demonstrated the deformity to be a forward bowing of the gladiolus of the sternum and adjoining cartilages. The summit of the bow was at the level of the fourth costal cartilage. There was no evidence of beading at the costochondral junctions. From the fourth to the seventh costal cartilages the interspaces were very narrow and the cartilages appeared to converge toward the summit of the bow. The diaphragm appeared long in its anteroposterior diameter. (See Fig. 4) The tendinous portion instead of being trefoil in shape took the form of a V with its apex reaching the xiphoid process. Just lateral to this apex the musculature portion was very thin and its muscle fibers poorly developed. In fetal life this area develops from the septum transversum. The point at which this portion of the diaphragm had fused with that derived from the pleuroperitoneal membrane was evident by a diagonal raphe extending to the central tendon. This lateral portion of the diaphragm contained the strongest and longest muscle fibers. The posterior muscular portion of the diaphragm was more developed than normal so that there was very little evidence of the vertebrocostal trigone on either side. In comparison to the normal diaphragm, the ratio of the muscular portion to the membranous portion was greater. These points of difference are obvious when the two diaphragms shown in Figures 3 and 4 are compared. Thus far, it has been shown that during life paralyzing the diaphragm interrupted the mechanism that produced the deformity and the postmortem findings of the diaphragm demonstrated that there is a departure from the normal structure of a diaphragm of a normal thorax.

## Discussion of the Diaphragmatic Theory

The suggested causes of congenital chondrosternal prominence have included rickets, respiratory obstruction and prolonged and severe cough and dyspnea resulting from cardiorespiratory affections. Rickets has been assumed to be responsible for almost all bony chest deformities without scientific basis. In this case, there was no evidence of rickets as shown by the blood chemistry. Obstructions in the respiratory tract, such as large adenoids and tonsils, are very common in infants although the deformity is comparatively rare and appears in 0.06% of children. In the vast majority of children that suffer severe and prolonged cough or dyspnea, there is no evidence of this type of deformity. In addition, the deformity is more manifest and appears to be affected by the inspiratory contraction of the diaphragm. When the diaphragm is paralyzed, as was demonstrated in the previously described test, the mechanism that appears to create the deformity stops. The deformity first makes its appearance in the early months of infancy and progresses as the child grows older. Many authors believe that the reverse deformity (congenital chondrosternal depression) results from a congenital developmental defect in the structure of the diaphragm. In the normal thorax during inspiration there is a state of equilibrium in the contracted ring of musculature of the diaphragm so that there is no greater pull on any one point of the lower chest. In the case of congenital costochondral sternal depression this equilibrium is disturbed so that there is a strong inward pull on the gladiolar-xiphoid junction where the greatest depth of the depression occurs. This is believed to be caused by a shortened anterior central tendon.

In the case of congenital chondrosternal prominence, the anterior central portion of the membranous diaphragm was seen to be elongated and to contain comparatively few muscle fibers. Just lateral to each membranous limb of the inverted V of the tendinous portion of the diaphragm the muscular portion is most strongly developed and contains the longest fibers. (Fig. 4) The origin of this muscular portion is directly under the Harrison's groove for which it is believed to be responsible. It was very noticeable that when the diaphragm was paralyzed on one side the corresponding Harrison's groove was not deepened on inspiration. It can, therefore, be concluded that the contraction of such a diaphragm during inspiration results in a retraction of the lower anterior chest along

Harrison's groove and of the epigastric portion of the abdominal wall. This mechanism is believed to be responsible for the gradual evolution of this deformity.

In further support of this diaphragmatic theory, neither of the chondrosternal deformities are seen at birth. They always are said to have been noticed shortly after birth after the diaphragmatic action has been exerting its effect for that period. Based on these facts one can state a hypothesis; namely, given a congenital chondrosternal abnormality there must be an abnormal diaphragm.

## Conclusion

A new term congenital chondrosternal prominence is suggested for the chest deformity referred to by various names as pigeon breast, pectus carinatum, piriform breast, etc.

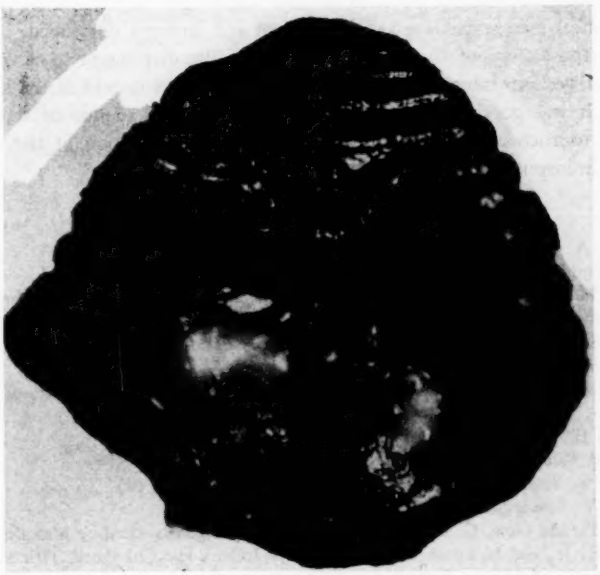

Fig. 5. Thorax and diaphragm of four-week-old dog with typical chondrosternal depression (funnel chest). Note absence of anterior portion of diaphragm which includes the anterior leaf and the sternochondral muscular portion of diaphragm.

The present concepts of the eiology of this deformity are discussed. Causative factors, such as rickets, upper respiratory obstructions, and severe prolonged cough and dyspnea are questioned and a new theory is advanced.

A case of congenital chondrosternal prominence is presented and the diaphragmatic theory is advanced as the etiologic factor. Postmortem examination of the diaphragm is described and the relationship between the embryologic development of the diaphragm and the deviation from the normal anatomy is pointed out. Departure from the normal development of the diaphragm is held responsible for the congenital anterior chest deformities as congenital chondrosternal depression (funnel chest), congenital chondrosternal prominence (pigeon chest) and chondrocostal depression (Harrison's grooves).

## Addendum

The author was fortunate in obtaining the body of a four week old suckling dog that had a congenital chondrosternal depression (funnel chest). The dog was killed because of congenital malformation of both forelegs. The lungs and heart were normal. After dissecting the thoracic cage and diaphragm, the chest deformity was found to conform exactly to that seen in humans. Inasmuch as no diaphragm with this deformity has been previously reported, its description is most timely and important.

The most obvious difference is, instead of a trefoil membranous portion seen in normal diaphragm, the anterior leaf which is formed from the septum transversum is absent. (Fig. 5.) The two lateral leaves are fused anteriorly. The anterior margin of the fused membranous portion of the diaphragm is attached to the sternal muscle at the sternoxiphoid junction. The lateral portions of the diaphragm which are derived from the pleuroperitoneal membranes are very prominent and strongly developed. It may be concluded that the failure of the anterior portion of the diaphragm to develop from the embryological septum transversum is the cause of the development of the chondrosternal depression. It was previously attributed to a "short central tendon of the diaphragm." Contraction of such a diaphragm produces a paradoxical motion of the anterior chest wall so that in inspiration it is drawn in.

## References

1. Mitchell, A. G., and Nelson, W. E., Textbook of Pediatrics, 4th ed., W. B. Saunders Co., Philadelphia, Pa., 1945, p. 1182.
2. Brodkin, H. A., Congenital chondrosternal depression (funnel chest) relieved by chondrosternal neoplasty, Am. J. Surg. **75**:716, 1948.
3. Griffith, J. P. C., and Mitchell, A. G., Textbook of Pediatrics, 3rd ed., W. B. Saunders Co., Philadelphia, Pa., 1941, p. 833.
4. Marques, A., Torax piriforme en un caso de tetralogia de Fallot Hospital Rio de Janeiro **22**:47, 1942.
5. Eichhorst, H., Traite de Diagnostique Medical, cited by Marques (4).
6. Schiassi, F., Cited by Marques (4).
7. DeCastro, F., Tratado de Clinica Propedentica, cited by Marques (4).
8. Romeiro, V.,Semilogica Medica, cited by Marques (4).
9. Horden, T., and Gow, G. E., Essentials of Medical Diagnosis, cited by Marques (4).
10. Holt, L. E., Jr., and McIntosh, R., In Diseases of Infancy and Childhood, 11th ed., D. Appleton Co., New York, 1940, p. 298.
11. Brennemann, J., Practice of Pediatrics, Vol. 2, W. F. Prior Co., Hagerstown, Md., 1937, p. 64.
12. Graham, E. A., Singer, J. J., Ballon, H. C., Surgical Diseases of the Chest, Lea and Febiger, Philadelphia, Pa., 1935, p. 67.
13. McCormick, J., Personal Communication.
14. Blalock, A., Personal Communication.
15. Arey, L. B., Developmental Anatomy, 3rd ed., W. B. Saunders Co., Philadelphia, 1938, p. 238.
16. Best, C. H., and Taylor, N. B., Physiological Basis of Medical Practice, 4th ed., Williams and Wilkins Co., Baltimore, Md., 1945, p. 302.

## Spanish Abstract

### Prominencia Condroesternal Congénita (Pecho de Paloma)

A las deformidades del pecho tales como pecho de embudo y pecho de paloma se les ha dado nombres sugestivos de gran aspecto. El autor las clasifica como congénitas y sugiere los nombres "depresión condroesternal congénita" para el pecho de embudo, "prominencia condroesternal congénita" para el pecho de paloma, y "depresiones condrocostales congénita para los surcos de Harrison.

Otros han atribuído estas deformidades al raquitismo, a obstrucciones respiratorias superiores, compresiones intrauterinas, tos y disnea severas y prolongadas.

El autor presenta una nueva teoría etiológica: 1o. se le da énfasis al factor congénito; 2o. se llama la atención al hecho de que el diafragma es el órgano principal de respiración durante los primeros meses de vida y el factor principal en moldear la forma normal del pecho; y 3o. estudio del desarrollo embriológico del diafragma indica que la desviación o alteración en fusión de sus componentes puede alterar su contracción muscular y así afectar particularmente el asimiento costocondroesternal. Sosteniendo la teoría, se mencionan resultados de tratamiento quirúrgico en depresión condroesternal congénita. En un caso de prominencia condroesternal congénita, el diafragma se paraliza por medio de inyección de 1% de novocaína en el nervio frénico, y se arresta el mecanismo que produce la deformidad.

Se describe un caso de prominencia condroesternal congénito, dando énfasis a las características de la deformidad. Se describen la configuración del diafragma, la proporción y distribución de la porción muscular y la porción tendinosa que afectan la respiración. Se concluye que la alteración congénita en el desarrollo del diafragma resulta en el acento anormal en ciertos asimientos a la orilla inferior anterior de la caja torácica tan pronto como la respiración principia. Esto interfiere con su evolución normal de la forma redonda a la epilíptica durante el primer año de vida, resultando en una depresión a prominencia torácica, dependiendo de variaciones en la porción muscular circunferencial del diafragma.

*365 Osborne Terrace.*

# GENERALIZED NON-FATAL HISTOPLASMOSIS IN AN INFANT

*By* RICHARD W. BLUMBERG, M.D., ISAAC RUCHMAN, PH.D., AND RALPH J. JOHANSMANN, M.D.
*Atlanta, Ga.*

FOLLOWING Smith's[1] suggestion that histoplasmosis may be responsible for the pulmonary calcifications found in certain individuals with negative tuberculin tests, considerable evidence of a circumstantial nature has accumulated which supports his view.[2-4] According to the adherents of this concept there must exist a benign form of histoplasmosis, the end stage of which is often represented by pulmonary calcifications. However, generalized histoplasmosis was always considered a fatal disease until Bunnell and Furcolow[5] recently reported two cases with apparent recovery and one in which recovery seems probable. Several instances of recovery from localized mucocutaneous lesions have been reported.[6,7]

It is the purpose of this paper to report another instance of proved systemic histoplasmosis with apparent recovery, and to add further observations on the cutaneous reaction to histoplasmin and other fungus antigens. Details of cultural technic are included.

## CASE REPORT

M. L. C., a 2-month-old Negro girl was admitted to the Children's Hospital because of an enlarged liver and spleen. She had been well until two days prior to admission, when she developed a nasal discharge, cough, irritability, and seemed warmer than usual. Because of these complaints she was taken to a neighborhood clinic where physical examination revealed an enlarged liver and spleen, in addition to evidence of infection of the upper respiratory tract. She was referred to the hospital for further study.

She was a full term infant, firstborn, in Fayetteville, Tenn. Birth weight was 3.2 kg. Feeding had been by breast exclusively and no vitamin supplements had been offered. She had vomited about once a day, usually soon after one of her feedings. A fine papular eruption, noted on the face at 6 weeks of age, disappeared after the local application of some ointment. The family moved from Tennessee to Cincinnati when the patient was seven weeks old.

The patient's mother, 19 years old, gave a history of having had a syphilitic infection at the age of 16 years. She had been inadequately treated at the time but received weekly injections, both intramuscularly and intravenously, for 6 months, beginning with the first month of her pregnancy. A Kahn test performed while the patient was hospitalized was negative.

Physical examination on admission revealed a well developed, well nourished, irritable Negro girl, not acutely ill. Body temperature was 37.4C. Weight was 4.4 kg. Positive findings were a mucoid nasal discharge and an enlarged, firm, non-tender liver and spleen. Liver edge was palpable 4 finger-breadths inferior to the RCM, and the spleen, 3½ finger-breadths inferior to the LCM anteriorly. There was no lymphadenopathy.

Initial examination of the blood revealed: RBC 3.4 million/cmm., Hgb. 8 gm./100 cc., and WBC 9.9 thousand with a differential cell count of leukocytes 49%, lymphocytes 35%, monocytes 14%, and myelocytes 2%. Two normoblasts were found. Urine showed a 4 plus reaction for albumin. Microscopic examination was negative. Blood chemical studies on admission revealed:

---

From The Children's Hospital Research Foundation and the Departments of Pediatrics, Bacteriology and Pathology, College of Medicine, University of Cincinnati, Cincinnati, Ohio.

(Received for publication July 15, 1948.)

NPN 30 mg., phosphorus, 2.5 mg., total protein 5 gm., of which 2.6 gm. was albumin and 2.4 gm. was globulin/100 cc. serum. Serum phosphatase was 11.5 Bodansky units, and cephalin-flocculation test gave a 4 plus reaction. Blood was drawn for culture.

Course in the hospital was uneventful except for an increasing degree of anemia and a persistent low-grade fever. Liver and spleen remained essentially unchanged in size. RBC remained around 3.0 million/cmm. and Hgb., 7-8 gm./100 cc. Body temperature ranged from 37.2C. to 37.8C., and occasionally rose to 38.3C.

Numerous laboratory studies were made. In addition to the admission blood culture, repeat blood cultures were taken on the 2nd, 4th, and 14th days. Cultures of the nose and throat revealed Staph. aureus hemolyticus and green streptococci. Stool and urine cultures were negative. A fresh blood preparation revealed no evidence of sickling. Agglutinations against Br. melitensis, Br. abortus, and Past. tularensis were negative. Spinal fluid was normal. Wassermann and Kahn tests were negative

TABLE I

RESULTS OF SKIN TESTS IN PATIENT WITH HISTOPLASMOSIS

| Skin test reagent (0.1 cc. intracutaneously) | M. L. C. Histoplasmosis 2/22/47 | M. L. C. Histoplasmosis 5/22/47 | J. E. Control 5/22/47 |
|---|---|---|---|
| Histoplasmin (old lot)† | 0 | (1.1+)# | 0 |
| Histoplasmin (new lot)† | — | (0.9+) | 0 |
| Histoplasmin* | — | (0.9+) | 0 |
| Histoplasma vaccine 1:5000* | — | (0.5)+ | 0 |
| Monilia albicans* | — | 0 | 0 |
| Blastomycin* | — | 0 | 0 |
| Coccidioidin* | — | 0 | 0 |
| Histoplasma rabbit serum—undiluted* | — | 0 | 0 |
| Histoplasma rabbit serum—diluted 1:10* | — | 0 | 0 |
| Normal rabbit serum—undiluted | — | 0 | 0 |
| Normal rabbit serum—diluted 1:10 | — | 0 | 0 |

† Material furnished through the courtesy of Dr. J. C. Peterson.

# Figure in parentheses denotes greatest diameter in centimeters.

* Material kindly supplied by Dr. Norman F. Conant.

in the patient and in both parents. Toxoplasma neutralization tests performed with sera from the patient and both parents were also negative. A tuberculin test, employing 0.0005 mg. of PPD, was negative. A histoplasmin skin test with a 1:100 dilution of the antigen gave no reaction. However, the father and mother's skin tests were markedly positive with the same strength antigen.

Roentgenograms of the skull, long bones, and the chest on admission were normal. Reexamination of the chest 5 days later revealed a slight amount of peribronchial infiltrate on the right side. No calcifications were noted.

On the 3rd day a biopsy of the bone marrow was performed. Material was obtained for direct examination, culture, and histologic examination. On the 6th day a liver biopsy was performed. Details of these studies are presented elsewhere but both were positive on culture for Histoplasma capsulatum. The blood culture obtained on the day of admission also yielded Histoplasma capsulatum.

Treatment was entirely symptomatic. Three transfusions of whole blood were given after the diagnosis was established. The child ate well, and gained a slight amount in weight. On the 18th day, when discharged to be followed in the out-patient clinic, her RBC numbered 4.14 million with Hgb. 11 gm./100 cc., and WBC, 4.7 thousand with a normal differential cell count.

Three weeks after dismissal from the hospital, and 6 weeks after the onset of the illness, the child was seen again. There had been a slow but progressive gain in weight and the body temperature was normal. The liver and spleen remained unchanged in size. The blood picture was the same

as at the time of discharge except that the WBC numbered 3.3 thousand with a normal differential count.

At 4 months of age she was brought to the Hospital again because of a cough of one week's duration. The child appeared acutely ill, and had a temperature of 38.8C. Severe paroxysmal coughing followed by vomiting was observed and coarse rhonchi were heard throughout both lung fields. The liver was still palpable 4 finger-breadths and the spleen, 3 finger-breadths inferior to the R and LCM respectively. Both were firm and nontender. A diagnosis of pertussis was made and the child was admitted to the contagious disease unit of the Cincinnati General Hospital. Admission blood studies revealed WBC 29 thousand/cmm. with a differential count of polynuclears 12%,

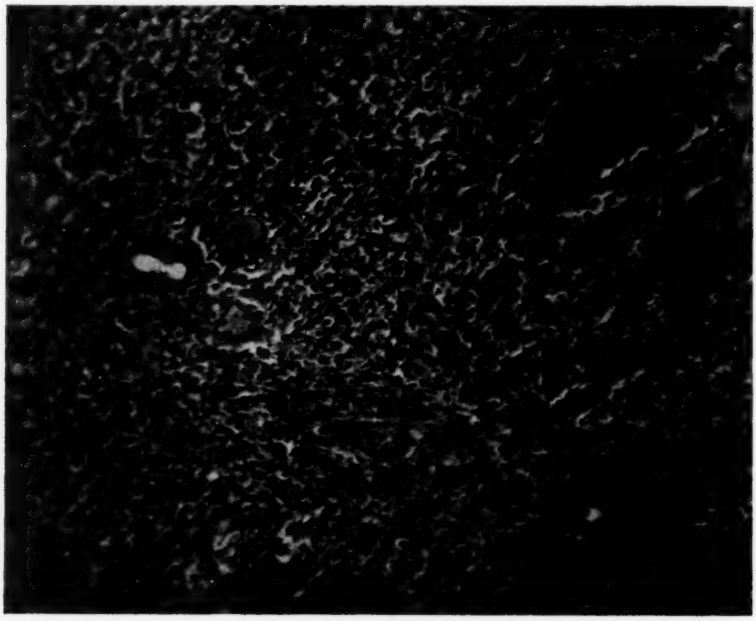

FIG. 1. Photomicrograph of liver showing chronic inflammation of a portal canal and hepatic lobule. Hematoxylin and eosin. X 160

eosinophiles 4%, lymphocytes 80%, and monocytes 4%. She was discharged 26 days later much improved. The course of the illness was apparently modified by the use of hyperimmune human pertussis serum. A repeat histoplasmin skin test done at this time, 3 months after her first test, was positive. Other skin tests employing various fungal antigens, performed simultaneously were negative (Table I).

On repeated visits to the out-patient clinic it was observed that the liver and spleen, although still enlarged, were receding in size. The child ate well and had grown and gained in weight remarkably well. When last observed, at the age of 16 months, she weighed 9.5 kg. The liver was palpable, 1½ finger-breadths, and the spleen only 1 finger-breadth inferior to the R and LCM respectively. Both were still firm. The most recent X-ray film of the chest, taken one year after onset of the infection, shows a normal chest with no evidence of calcification.

Sera obtained on July 1, 1947, and March 10, 1948, were found to fix complement strongly.*

* The complement-fixation tests were performed by Dr. M. L. Furcolow, U. S. Public Health Service, Kansas City, Kan.

### Laboratory Data

*Liver Biopsy:* At laparotomy the liver was large, firm and reddish-brown and was peppered with numerous tiny light gray areas. Microscopic sections of a small piece obtained by biopsy (Fig. 1) showed the presence of a marked chronic granulomatous inflammatory reaction which distorted the lobular architecture. The inflammatory response was composed of lymphocytes, macrophages, eosinophiles and a few foreign body giant cells of the Langhans type and was accompanied by slight connective tissue proliferation and fibrosis. It was distributed rather irregularly throughout the specimen but predominantly involved the portal canals from which points it streaked out into the surrounding hepatic lobules, principally between the hepatic cords. There was slight bile duct reduplication in a few of the portal canals. Occasional tiny discrete tubercular lesions occurred in the infiltrate in and around the portal canals and in the mid or central portion of the hepatic lobules. They were composed of a collection of macrophages and connective tissue cells and sometimes contained

TABLE II

Results of Examination of Patient's Tissues for Presence of Histoplasma Capsulatum

| Patient's tissues examined | Day of disease | Direct smear or sections | Culture | | | Mouse inoculation |
|---|---|---|---|---|---|---|
| | | | Trypticase soy bean broth | Blood agar | Sabouraud's agar | |
| Blood | 3 | 0 | + | - | - | - |
| | 4 | - | 0 | 0 | - | - |
| | 8 | - | 0 | 0 | - | - |
| | 16 | - | 0 | - | 0 | - |
| | 41 | - | 0 | - | 0 | - |
| | 97 | - | 0 | 0 | 0 | - |
| Spinal fluid | 5 | - | 0 | 0 | - | - |
| Bone marrow | 5 | 0 | - | + | + | + |
| Liver biopsy | 8 | 0 | - | + | + | + |

one or more foreign body giant cells. Occasionally a foreign body giant cell appeared isolated in a liver lobule. There was degeneration of the hepatic cells adjacent to the inflammatory sites and a few cells contained droplets of fat. Clusters of immature cells of the erythroid series appeared in the unaffected portions of the liver lobule and here the majority of the hepatic cells appeared to be filled with glycogen. No Histoplasma capsulatum or other organisms were visible in the lesions or in impression smears prepared on fresh material at the time of operation.

*Bone Marrow Biopsy:* Microscopic sections of a small clot of bone marrow aspirated from the tibia revealed several submiliary tubercular lesions composed of an aggregation of epithelioid cells, proliferating connective tissue cells and a few lymphocytes. A few of the tubercles contained a centrally situated foreign body giant cell of the Langhans type. There was no caseation. No organisms were demonstrated in these lesions.

### Cultivation

Blood taken 3 days after the onset of illness, bone marrow aspirated on the 5th day and material from the liver biopsy performed on the 8th day showed the presence of Histoplasma capsulatum either by cultivation in various media or by inoculation into mice or by both methods (Table II).

*Blood:* The blood obtained on the day of the patient's admission to the hospital was inoculated into trypticase soy bean broth. Growth of the mycelial form of Histoplasma capsulatum became apparent after the first week. Continued incubation resulted in the formation of the large tuberculate

chlamydospores microscopically characteristic of Histoplasma capsulatum (Fig. 2). Subinoculation of the growth to other media yielded the mycelial form of the organism on Sabouraud's agar and the yeast-like phase on sealed blood agar plates (Fig. 3). Organisms were not recovered from subsequent blood cultures drawn between 4 and 97 days after onset of illness.

*Spinal Fluid:* Spinal fluid obtained 3 days after admission was inoculated into trypticase soy bean broth and onto blood agar plates but no growth occurred.

*Bone Marrow:* Bone marrow was obtained for study 3 days after admission. The material was ground in a mortar with 2 cc. of physiologic saline and 0.3 cc. was injected intraperitoneally into each of 6 mice. The remainder was streaked on Sabouraud's agar and blood agar plates. One pair of Sabouraud's and blood agar plates was kept at room temperature while another pair was sealed with

Fig. 2

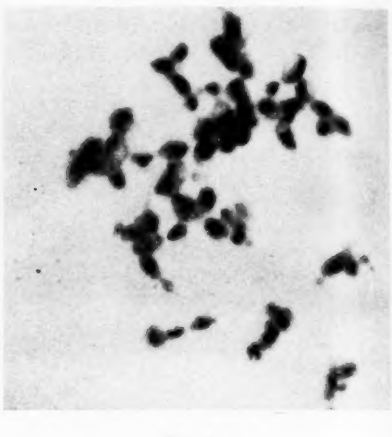

Fig. 3

FIG. 2. Mycelial phase of Histoplasma capsulatum. Methylene blue. X 300
FIG. 3. Yeast-like phase of Histoplasma capsulatum. Wright's stain. X 1000

"parafilm" to prevent drying and kept at 37°C. Growth appeared on all four plates within about 2 weeks but the maximal number of colonies appeared on the Sabouraud's agar stored at room temperature.*

Six mice inoculated with the bone marrow suspension remained well. Two were sacrificed at the end of one month and a suspension of a pool of their livers and spleens was streaked on blood agar plates. A set of sealed and unsealed plates was kept at room temperature while a second set was incubated at 37°C. Good growth of Histoplasma capsulatum was obtained on all plates. Two more mice were sacrificed at 6 weeks and organisms in the yeast-like phase were readily demonstrated in histologic sections of their spleens. Culture of a suspension of the spleens resulted in growth of the yeast-like phase of Histoplasma capsulatum on sealed agar plates and the mycelial phase on Sabouraud's agar. The remaining two mice were allowed to survive.

*Liver:* The pieces of liver obtained at biopsy were ground in a mortar with 1 cc. of saline. Part of the suspension was inoculated into mice—0.2 cc. intravenously into each of 2 mice and 0.2 cc. intraperitoneally into 2 additional mice. The remainder was spread over the surfaces of 2 blood agar plates. One plate was kept at room temperature and the other at 37°C. Histoplasma grew out on both plates. One of the mice injected intravenously died after 6 weeks and a Wright's stained smear of its spleen revealed the presence of Histoplasma capsulatum in the yeast-like phase. The second mouse, after a chronic illness, died in about 2 months but a search for organisms was not made. The 2 mice inoculated intraperitoneally have remained well for more than 6 months.

Although an extensive investigation was not done it became apparent that this strain of histoplasma grew better at room temperature than at 37°C. Furthermore, this occurred not only upon initial isolation but after a few subcultures as well.

* The identity of Histoplasma capsulatum was confirmed by Dr. Lee Foshay.

## Discussion

The apparent recovery of another patient (the third reported) from a proved systemic infection with Histoplasma capsulatum presents additional evidence that the generalized form of the infection is not uniformly fatal. There is now proof[5] that the infection may exist with varying degrees of severity, ranging from the mild form, as exemplified by our patient, to the more commonly recognized fatal form. Our patient was brought to a well-baby clinic because she was thought to have a "cold," and was hospitalized only because an enlarged liver and spleen were detected on routine physical examination. At no time did she appear very ill and no therapy was administered which might have altered the course of her disease. Had her parents been less careful, she would undoubtedly have had her infection and recovered without the diagnosis' having been made.

The basis of much of the previously reported circumstantial evidence in favor of a benign form of histoplasmosis has been the histoplasmin skin test. Emmons, Olson, and Eldridge[8] have cast considerable doubt upon the specificity of the test by the demonstration of cross sensitivity between histoplasmin and other fungus antigens in animals experimentally infected with various fungi. The reaction of the patient reported here when tested with histoplasmin and other fungus antigens is of considerable interest. The histoplasmin test was negative when first performed at the age of two months during the early stage of the disease. At this time the patient was in relatively good physical condition, did not appear ill, and had little or no temperature elevation. When tested 90 days later she reacted both to the same preparation of histoplasmin used previously and to another preparation of comparable strength obtained from a different source. It would, therefore, seem probable that at the time of the first test, while the blood culture was positive, she was in an anergic or pre-allergic state, such as is often seen early in tuberculous infections.

This same change in skin sensitivity from negative to positive was also observed by Bunnell and Furcolow[5] in three of their patients. Two had high fever and clinically appeared severely ill, while the third had been ill only three weeks at the time of the first negative test. They were found to be histoplasmin positive when repeat tests were performed at intervals of 35, 46, and 85 days. A similar change from a negative to positive skin test was noted by Curtis and Grekin[7] in one of their patients who had a proven infection with Histoplasma capsulatum.

No positive skin reactions were elicited when our patient was tested with other fungus antigens (see Table I). Bunnell and Furcolow found only one instance of reaction to another fungus antigen, blastomycin, in the four patients with histoplasmosis who were similarly tested with a variety of fungus antigens. When the histoplasmin and blastomycin were diluted further only the histoplasmin produced a reaction in their patient. The failure to demonstrate cross sensitivity in our patient and in the four reported by Bunnell and Furcolow suggests that there is less tendency to cross reactions in humans than in experimentally infected animals.

Histoplasmin skin tests have been previously reported in only 20 patients with proved histoplasmosis.[2, 5, 7, 9–14] Only eleven responded with a positive reaction. In an additional patient, the results of the test were considered equivocal. Of the nine patients with negative reactions eight could be considered to be in the terminal stage of the disease at the time of the test. It is of interest that in five instances in which the patient's skin test was negative, the histoplasmin test in the parents was positive. This was also observed in our case.

Where the diagnosis of histoplasmosis is suspected, reliance should not be placed on one diagnostic procedure alone. Only the initial blood culture performed in our patient was positive. Histologic examination of tissue removed by liver and bone marrow biopsy failed to reveal the presence of organisms although culture and animal inoculation of this material readily grew out Histoplasma capsulatum. The recently described complement fixation test[15, 16] for histoplasmosis seems to provide confirmatory evidence that the patient has been infected by Histoplasma.

## Summary

A case of systemic infection with Histoplasma capsulatum with recovery is reported. The organisms were recovered from the blood, bone marrow, and liver. No specific therapy was administered.

Change in skin sensitivity to histoplasmin from negative in the early stage to positive in the convalescent stage was noted. No cross reactions with various other fungus antigens were observed.

## References

1. Smith, C. E., Coccidioidomycosis, M. Clin. North America **27**:790, 1943.
2. Christie, A., and Peterson, J. C., Pulmonary calcification in negative reactors to tuberculin, Am. J. Pub. Health **35**:1131, 1945.
3. Palmer, C. E., Nontuberculous pulmonary calcification and sensitivity to histoplasmin, Pub. Health Rep. **60**:513, 1945.
4. Christie, A., and Peterson, J. C., Histoplasmin sensitivity, J. Pediat. **29**:417, 1946.
5. Bunnell, I. L., and Furcolow, M. L., Report on ten proved cases of histoplasmosis, Pub. Health Rep. **63**:299, 1948.
6. Strong, R. P., Study of some tropical ulcerations of skin with particular reference to their etiology, Philippine J. Sc. **1**:91, 1906.
7. Curtis, A. C., and Grekin, J. N., Histoplasmosis, J.A.M.A. **134**:1217, 1947.
8. Emmons, C. W., Olson, B. J., and Eldridge, W. W., Studies of role of fungi in pulmonary disease; cross reactions of histoplasmin, Pub. Health Rep. **60**:1383, 1945.
9. Van Pernis, P. A., Benson, M. E., and Holinger, P., Specific cutaneous reactions with histoplasmosis, J.A.M.A., **117**:436, 1941.
10. Parsons, R. J., and Zarafonetis, C. J. D., Histoplasmosis in man, Arch. Int. Med. **75**:1, 1945.
11. McLeod, J. H., Emmons, C. W., Ross, S., and Burke, F. G., Histoplasmosis, J. Pediat. **28**:275, 1946.
12. Iams, A. M., and Keith, H. M., Histoplasmosis in infancy, J. Pediat. **30**:123, 1947.
13. Davis, H. V., and Neff, F. C., Histoplasmosis in infancy, Am. J. Dis. Child. **71**:171, 1946.
14. Miller, H. E., Kiddie, F. M,, Johnstone, H. G., and Bostick, W. L., Histoplasmosis, Arch. Dermat. & Syph. **56**:715, 1947.
15. Salvin, S. B., Complement fixation studies in experimental histoplasmosis, Proc. Soc. Exper. Biol. and Med. **66**:342, 1947.
16. Furcolow, M. L., Bunnell, I. L., and Tenenberg, D. J., Complement fixation test for histoplasmosis; preliminary results with human sera, Pub. Health Rep. **63**:169, 1948.

## Spanish Abstract

### Histoplasmosis Generalizada no Fatal en un Infante

Se reporta un caso de infección general orgánica con Histoplasma capsulatum que se alivió. Los organismos fueron recobrados de la sangre, de la médula de los huesos y del hígado. No se administró terapia especifica.

Se notó un cambio en la sensibilidad de la piel a la histoplasmina, de negativa en los primeros estados a positiva en el estado convalesciente. No se observaron reacciones atravesadas con otros antígenos de fungosidad.

*33 Ponce de Leon Ave., N.E.*

# ENCEPHALITIS: ISOLATION AND IDENTIFICATION OF VIRUS FROM BODY FLUIDS OF HUMAN SUBJECTS

*By* RUSSELL J. BLATTNER, M.D., AND FLORENCE M. HEYS, PH.D.
*Houston, Texas*

PATIENTS presenting signs and symptoms suggesting virus infection of the central nervous system offer a difficult problem in differential diagnosis. Exact etiologic diagnosis cannot be made with certainty on clinical grounds alone. While spinal fluid findings may be helpful, it is necessary to resort to specialized laboratory procedures for assistance in determining etiology. In general, two diagnostic methods are available: (1) Isolation and identification of virus from body fluids of the patient; (2) Demonstration of increasing humoral antibody titer to a known virus during clinical recovery. Neutralization tests, and complement fixation and agglutination procedures have been utilized to good advantage. If autopsy material should become available, pathologic and biologic study of postmortem tissue is often helpful in establishing the etiology.

About 10 years ago at the Children's Hospital in St. Louis we began routine study of patients showing manifestations suggesting central nervous system involvement, with a view to exact etiologic diagnosis. The routine clinical procedure on these patients included spinal fluid studies such as cell count with differential, sugar and protein determinations, bacterial culture and usually blood sugar, simultaneous with spinal fluid sugar. Those patients for whom bacterial etiology, pyogenic or acid fast, was established, were eliminated from this particular study. Those patients having central nervous system involvement including spinal fluid changes, for whom no bacteriologic etiology could be established, were considered to have possible virus infections. Fluids from the latter were subjected to special laboratory procedures: (1) studies with heparinized blood; (2) studies with spinal fluid; (3) studies with blood sera.

The usual procedure in attempting isolation of virus from blood was as follows: heparinized blood taken at varying intervals after onset of clinical symptoms, was inoculated into white Swiss mice and onto the retracted chorioallantois of embryonated hen's eggs.

In the period from 1943-1947, samples of heparinized blood from 81 patients suspected of having encephalitis were studied in this manner for the presence of virus. Table I shows the distribution of these cases by year and month.

Of these attempts virus was recovered in one instance only. A filterable virus was isolated from the peripheral blood of an eight-year-old boy seen at St. Louis Children's Hospital during the early part of July 1945.[1] Peripheral blood drawn on the fifth day of illness was inoculated intraperitoneally, 0.05 ml., into each of six white Swiss mice, nine days of age. Signs of illness appeared in these mice on the seventh day following inoculation. Virus was recovered from the brain tissue of these young mice, and was established readily in adult white Swiss mice by intracerebral passage. The infectious

From the Department of Pediatrics, Baylor University College of Medicine.

Read before the joint meeting of the American Pediatric Society and the Canadian Society for the Study of Diseases of Children, Quebec City, May 26, 1948.

(Received for publication June 3, 1948.)

agent was identified by appropriate tests as the virus of St. Louis encephalitis. It is worthy of note that no virus was isolated from the spinal fluid which was inoculated at the same time as the heparinized blood, into six litter mates of the nine-day-old mice used for the inoculation of the blood. Likewise intraperitoneal and intracerebral inoculation of adult white Swiss mice with the same sample of heparinized blood, from which virus isolation was successful in young mice, failed to demonstrate its presence. Previous experience has shown that young mice, which may be inoculated while still with the mother, are extremely susceptible to small quantities of virus.

During clinical recovery this patient developed increasing titer of type specific antibody to a stock strain of the virus of St. Louis encephalitis (Hubbard) and to the strain newly isolated from his blood stream.

Thus, of 81 attempts, a filterable virus was isolated and identified in one instance. In

TABLE I

PERIOD FROM 1943 TO 1947. STUDIES WITH HEPARINIZED BLOOD FROM EIGHTY-ONE PATIENTS. DISTRIBUTION BY YEAR AND MONTH.

| Year | Total | Jan. | Feb. | Mar. | Apr. | May | June | July | Aug. | Sept. | Oct. | Nov. | Dec. |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1943 | 5 | | | | | | 2 | 2 | 1 | | | | |
| 1944 | 14 | | | | | | 2 | 4 | 3 | 2 | 1 | 1 | 1 |
| 1945 | 33 | 1 | | 2 | | 3 | 4 | 7 | 4 | 5 | 2 | 4 | 1 |
| 1946 | 25 | | 4 | | | | | 7 | 6 | 7 | 1 | | |
| 1947 | 4 | | | | 2 | 2 | | | | | | | |

so far as we have been able to ascertain, this isolation of the virus of St. Louis encephalitis from human blood during life represents the only such instance of isolation from a patient who recovered.

A series of 304 patients was studied for the presence of virus in spinal fluid. These patients were seen from 1940 through 1947, distribution by years being as follows: 14 in 1940, 25 in 1941, 41 in 1942, 57 in 1943, 58 in 1944, 60 in 1945, 42 in 1946 and seven in 1947. Of this number of spinal fluids studied, a virus was recovered in seven cases. The general procedure was as follows: as soon as possible after lumbar puncture, the spinal fluid sample was inoculated into white Swiss mice by intracerebral or intraperitoneal route, or both, and at the same time onto the retracted chorioallantois of embryonated hen's eggs. On rare occasions corneal inoculation in the rabbit was used for verification, and in an attempt to obtain positive evidence of virus in the shortest possible time.

Among these 304 cases, five strains of lymphocytic choriomeningitis virus were isolated. Four of the five cases occurred in January, February or March; the fifth occurred in September. Four of the five were children, ranging in age from six to 14 years, and the fifth was a young adult. The initial isolation of virus was accomplished in four instances by both egg and mouse inoculation, and once by egg inoculation only. In the latter instance two chorioallantoic passages were required to build up the titer of virus to a level sufficient to produce encephalitis in mice. During clinical course in all five patients, increasing titer of humoral antibody to a stock strain of lymphocytic choriomeningitis was demonstrated, as well as to the respective strain of virus isolated from the

patient. The virus of lymphocytic choriomeningitis was isolated also from wild mice trapped in the dwellings of two of the five patients reported here.

In one case of encephalitis following smallpox vaccination, a strain of vaccinia was recovered from blood-tinged spinal fluid taken on the 13th day following vaccination. This infant of nine months, who was seen in October 1946, developed signs of illness on the ninth day following vaccination: fever, drowsiness, vomiting. On the day of admission, which was the 13th following vaccination, there had been generalized convulsions. From the blood-tinged spinal fluid, the virus of vaccinia was recovered by chorioallantoic inoculation and by corneal inoculation in the rabbit. During the course of clinical recovery the patient's serum showed increasing titer of antibody to a known strain of vaccinia and to the newly recovered strain. Unfortunately, no attempt was made to isolate virus from the blood stream until the 19th day following vaccination, six days after the spinal fluid was found to be positive for virus. No virus was isolated from the blood. The patient recovered with no residuals. While the study of this case was of considerable interest, it does not follow necessarily that the post-vaccinal encephalitis was of virus etiology.

A strain of herpes virus (simplex) was isolated from the spinal fluid of a 14-year-old boy admitted to the St. Louis Children's Hospital on January 13, 1943. The patient expired on January 18, 1943. Three hours before admission, he had had a severe generalized convulsion. Past history was of interest in that this boy had never had herpes labialis, whereas his 15-year-old brother, who was his bed fellow, was subject to recurrent attacks of "fever blisters." The patient was admitted in a semi-stuporous state, but could be aroused for short periods during which he complained of headache. There was definite cervical rigidity, and neck flexion was painful. Reflexes were within normal limits, and no paralysis was noted. Brudzinski and Kernig signs were negative, and fundi were normal. The temperature which at the time of admission was 38.4°C., rose rapidly to 40°C. Respirations were 24/min. and pulse rate was 110/min.

Lumbar puncture on admission, 72 hours after probable onset of illness, yielded clear fluid showing 200 cells with acid, the majority of which were lymphocytes. Pandy was negative. Spinal fluid sugar was 74 mg.% with simultaneous blood sugar of 111 mg.%. Direct smear of the spinal fluid revealed no bacteria, and bacterial cultures, both aerobic and microaerophilic, were sterile. Subsequent lumbar punctures yielded spinal fluid samples giving positive Pandy and showing the presence of 290 to 420 cells, all lymphocytes.

Routine laboratory studies revealed urinalysis negative, Hglo. 15.3 gm., RBC 4.5 million, WBC 16,700, and a differential count of Stab cells 6, segmented cells, 73, lymphocytes, 19, mononuclear, 2. Tuberculin 1:1000 O.T., Wassermann and Kahn tests were negative. Routine agglutinations, including Proteus OX-19, Br. abortus, typhoid and paratyphoids A and B, were negative. Blood cultures were sterile, and routine throat culture showed only Staph. aureus.

The clinical course in this patient was steadily downhill, the temperature ranging from 39.5° to 40.6°C. He became increasingly more stuporous, and eventually lapsed into coma from which he could not be aroused. He expired on the fifth hospital day.

A spinal fluid sample taken on admission was inoculated almost immediately onto the retracted chorioallantois of embryonated hen's eggs (10 days' incubation). The inoculated membranes, which showed evidence of virus growth within 48 hours, were pooled and passed by intracerebral and intraperitoneal inoculation, 0.03 ml. and 0.1 ml., respec-

tively, to four young Swiss mice (four weeks of age). Within 12 days these mice developed mild convulsions. They were killed about two hours after the onset of convulsions. Autopsies revealed nothing unusual, and cultures in tryptose-phosphate broth of tissue from spleen, lung and brain were negative. The brain of each of these four mice was passed by intracerebral inoculation (0.03 ml.) to four mice, and in three to four days all of these secondary passage mice developed severe convulsions. In a similar manner the virus was recovered from a postmortem sample of spinal fluid.

Brain tissue taken at autopsy was studied for the presence of virus. A suspension (1:10) of brain tissue in tryptose-phosphate broth was inoculated intracerebrally, 0.03 ml., into six mice, three weeks of age. Within six days each mouse inoculated developed convulsions. Secondary passage established the strain in mice. Microscopic study of mouse brain tissue infected with these newly isolated strains of virus showed extensive encephalitic process and intranuclear inclusion bodies of the herpetic type.

Hamsters and guinea pigs inoculated with the original human brain suspension by combined intracerebral and intraperitoneal route showed no signs of illness over an observation period of three months.

The gross and microscopic findings in the brain of this patient were of particular interest. Dr. Margaret G. Smith, Associate Professor of Pathology at Washington University, made the following comments: "The only gross finding of significance was an area of softening in the medial inferior part of the left temporal lobe. Microscopic examination revealed that the pathologic lesions in the brain were limited to the olfactory regions. Necrosis was a prominent feature: necrosis of individual ganglion cells, and also more diffuse areas of necrosis ranging in size from 0.1 to 0.5 mm. In the area which appeared softened on gross examination, there were foci of necrosis almost a centimeter in diameter. These diffuse areas of necrosis occurred both in the cortical and the subcortical tissue, but were more extensive in the grey substance. Many ganglion cells contained eosinophilic intranuclear inclusions. Occasionally an intranuclear inclusion was present in glial cells. There was a mononuclear infiltration about many blood vessels. In contrast to the pathologic findings observed in other types of acute encephalitis, the characteristic changes in this case are extensive necrosis of brain tissue and the presence of intranuclear inclusions." The virus may have entered the central nervous system by way of the first nerve. The extensive involvement of the olfactory portion of the brain in contrast with the minimal involvement of other portions of brain suggests selective invasion of the pathways associated with the olfactory nerve.

A third series of studies concerned blood sera. From 1938 through 1946, 152 patients with clinical encephalitis, were studied for the development of type specific antibodies to the virus of St. Louis encephalitis. Mouse protection tests were carried out on serum samples taken during the course of clinical recovery, especially early and late in the course of the encephalitis. Seventeen of the 152 showed increasing titer of neutralizing antibody to the St. Louis virus. Of these 17 positives, two occurred in May, one in June, four in July, five in August, three in September and two in October. None of the clinical encephalitis cases shown to be of the St. Louis type, occurred in the winter months, an observation in contrast with that concerning lymphocytic choriomeningitis where four of the five positives occurred in the winter or spring months, January, February, March.

## Summary

Routine studies, for isolation and identification of the infectious agent, were made on patients showing signs of clinical encephalitis. The following results cover a period of about 10 years:

A strain of virus immunologically identical with the virus of St. Louis encephalitis was recovered from the peripheral blood. One of 81 attempts gave positive result, approximately 1%.

Seven strains of virus, comprising five of lymphocytic choriomeningitis, one of vaccinia and one of herpes simplex, were isolated from spinal fluid in 7 of 304 attempts, approximately 2%.

Increasing titer of type specific antibody to the virus of St. Louis encephalitis was demonstrated in 17 of 152 patients during the course of clinical encephalitis, approximately 1%.


## References


1. Blattner, R. J., and Heys, Florence M., Isolation of St. Louis encephalitis virus from the peripheral blood of human subject, J. Pediat. **28**:401, 1946.
2. Blattner, R. J., and Heys, Florence M., St. Louis encephalitis; occurrence in children in St. Louis area during nonepidemic years, 1939-1944, J.A.M.A. **129**:854, 1945.


## Encefalitis: Aislación e Identificación de Virus de Flúidos del Cuerpo de Sujetos Humanos


Se hicieron los estudios de rutina para la aislación e identificación de agentes infecciosos en pacientes que mostraron señas de encefalitis clínica. Los siguientes resultados abarcan un período de aproximadamente diez años:

Una cepa de virus inmunologicamente identica al virus de la encefalitis de St. Louis fué recobrada de la sangre periferal. Una de las 81 pruebas (aproximadamente 1%) dió resultado positivo.

Siete cepas de virus, comprendiendo cinco coriomeningitis linfocíticos, una de vacuna y otra de herpes simplex, fueron aisladas del flúido espinal en siete de las 304 pruebas. (Aproximadamente 2%).

El elevado título de anticuerpo específico del virus de la encefalitis de St. Louis fué demonstrado en 17 de los 152 pacientes durante el curso de encefalitis clínica. (Aproximadamente 1%).


*Baylor University College of Medicine*

# CYANOSIS IN INFANTS WITH NITRATES IN DRINKING WATER AS CAUSE

*By* WILL E. DONAHOE, M.D.
*Sioux Falls, S.D.*

THE cases reported here concern infants who have developed "blue spells" within a few weeks after leaving the hospital, or from two to seven weeks after birth, excluding cases of cyanosis due to pulmonary, cardiac, or central nervous system causes. Such cases have been referred to us as "idiopathic cyanosis," and satisfactory treatment depends upon recognition of the etiology of the cyanosis.

It has been assumed frequently that the thymus gland was the major cause of idiopathic cyanosis, and this structure has been the target for much radiotherapy. The patients herein reported had received from two to eight roentgen treatments prior to examination.

Stahr,[1] reported five cases of idiopathic cyanosis due to methemoglobinemia of unknown cause. Later, Rector and Schwartz[2] reported a similar case. Comly, published a report of two cases of methemoglobinemia and stated that it was due to nitrites derived from nitrates present in the drinking water. He included in his report seven other Iowa cases in which methemoglobinemia was presumed to have been present. The cyanosis disappeared in these seven cases after the use of the well water had been discontinued.

The presentation of these cases is intended to emphasize the possibility of contaminated drinking waters' being the cause of cyanosis in an infant, and to point out how this cause can be proved by withdrawal of the water without recourse to extensive and elaborate clinical or laboratory procedures.

## CASE HISTORY

Case 1. Infant B., aged 3 weeks, was brought to the hospital from its farm home in northwestern Iowa. The infant was deeply cyanotic. The color cleared within ten hours after admittance, following the administration of oxygen. The infant had been taken to another hospital on two other occasions because of cyanosis. Following three X-ray treatments there, the infant had returned home with normal coloring, only to have a gradual recurrence of the cyanosis. After a week in the hospital here, the cyanosis disappeared and the infant was dismissed. After being at home 10 days the baby became cyanotic again and was brought back. Oxygen was again administered and, after a short stay in the hospital, he was dismissed with the diagnosis of idiopathic cyanosis.

I learned later that the infant had been taken to a neighboring clinic, where four more X-ray treatments were given, and the infant had been normal ever since. While the baby was in the hospital, the parents had moved to another farm. The well of the vacated farm was found to be poorly constructed, shallow and considered "bad" by the neighbors. A presumptive lactose broth fermentation test of the water showed a marked contamination, and with brilliant green bile a partial confirmation of the Coliform group was made. Undoubtedly, this case of cyanosis was due to methemoglobin caused by the water nitrates.

Case 2. Infant B., aged 4 weeks, was brought in from southwestern Minnesota, because of a generalized marked cyanosis. The thymus gland had been treated previously, which supposedly cleared up an earlier spell of cyanosis. The baby was observed for a week, and returned to its home and former water supply with a diagnosis of idiopathic cyanosis. In about one week, blueness of the lips was noted. The water supply was changed immediately with no recurrence of blue spells. Water

(Received for publication May 11, 1948.)

analyses were not made, but it appears evident that the cyanosis in this case was due to the drinking water.

Case 3. Infant H. was brought in from northwestern Iowa. Shortly after birth, an X-ray treatment was given for a "possible thymus gland." This infant had suffered from erythroblastosis fetalis, was given three blood transfusions, and was discharged from the hospital at the age of six weeks. The infant returned two weeks later because of cyanosis. Oxygen therapy was used for a few hours and after a few days in the hospital, the patient was discharged. At home the baby's formula was made with the same well water, and the cyanosis of the lips and toes again became evident. On the ninth day, the infant was returned to the hospital, and in three days the cyanosis disappeared. Water samples were not obtained for nitrate determination, but specimens for the lactose broth fermentation test showed marked contamination with a presumptive Coliform group. The well itself was shallow and poorly constructed. At this time the home use of the water was discontinued, and the baby's coloring was normal for about six weeks. Then the parents, still skeptical about the deleterious effect of this well water, again gave it to the baby. Within a week the baby was brought in with slight cyanosis of the lips, fingers and toes. The parents confessed that they had again used their own water supply. This showed the development of cyanosis with three consecutive tests of contaminated water and the clearance of the cyanosis upon its discontinuance.

Case 4. Infant S., aged 6 weeks, was brought for examination from a farm in southwestern Minnesota. The child was born in the local hospital, and two weeks after its return home cyanosis of the lips, face, fingers and toes was noticed. The infant was returned to the hospital on two occasions, receiving X-ray treatments for an abnormal thymus gland, and dismissed each time after a few days, with normal coloring. In each instance, after a few days at home, cyanosis again appeared and with the third recurrence of cyanosis it became so generalized and intense that the baby was referred for consultation. Following 18 hours of hospitalization with consequent return to the normal coloring, the baby was sent home and the parents instructed to discontinue the further use of their own well water in the feeding of the baby. The formula and drinking water which the baby had previously received at home was from a shallow well, showing marked contamination with fermentation on lactose broth cultures and the presence of Coliform organisms. The nitrate content was 177 parts per million or the equivalent of 243 parts of sodium nitrate per million. Ten days later the infant was returned with slight cyanosis of the lips and finger tips, which the parents had noticed for several days. The father offered the explanation that the milk used in the infant's formula was from cows which drank the water from the home well. This time the milk from the cows as well as the water of the home place was discontinued. The baby had no more spells of cyanosis. A further test of giving the baby milk was not done, but it seems fair to assume that a baby might develop methemoglobinemia from such cow's milk.

Case 5. Infant S., aged 7 weeks, was brought for examination from southwestern Minnesota. The baby was born in a local hospital. A week after its return home it became quite cyanotic and was returned to the hospital where it was given an X-ray treatment for hypertrophy of the thymus gland. After a few days in the hospital, the color became clear and the child was returned home. A few days later the cyanosis again returned, and by the end of 10 days it had become generalized and very intense. Another physician was consulted at this time, an X-ray treatment was given at once, and the baby was referred to the author. Oxygen was administered for the cyanosis for a few hours, following admission to the hospital. There was no respiratory difficulty and the color cleared by the second day. The baby was discharged on the fourth day. The clearing of the cyanosis was attributed to the discontinuance of the home well water during the hospital stay. The well water showed contamination, with the presence of Coliform organisms and a nitrate content of 50 parts per million. This baby received no cow's milk or water from its own farm home well thereafter and had no recurrence of cyanosis.

## Comments

These five cases of cyanosis in early infancy, occurring in babies living on farms and clearing with withdrawal of drinking water contaminated with nitrates, emphasize the etiology. The water came from a well which had been in use for years without the occurrence of cyanosis in any other of the members of the family. It is difficult to explain why only an occasional infant develops cyanosis, why the nitrate content of the water

varies so greatly, and why it is not always the water with the highest nitrate concentration which causes cyanosis in the infant. Certain infants may have a low threshold to such poisoning or an idiosyncrasy to nitrites. Comly's[1] report also mentioned a survey of a number of Iowa farm wells by the Iowa State Planning Board, showing a varying nitrate content from zero to 125 parts per million. One sample revealed the extreme amount of 567 parts per million. The standards of safety set by the United States Public Health Service[2] allows for not more than 10 parts of N.P.N. per million. Water containing 10 or more than 15 or 20 parts N.P.N. per million might be potentially unsafe for infant consumption. This etiology in any case of cyanosis in an infant without adequate explanation can be demonstrated by changing the water for drinking or the formula. Laboratory tests of the blood or urine of the infant or water analysis may not be necessary. In such cases the infant is usually brought with marked cyanosis to the physician one to three weeks after leaving the hospital. While the parents describe the baby as having "blue spells," the dusky color was first noticed about the lips, then later about the fingers, toes, and face, eventually becoming generalized. While such cyanotic babies are restless, there is no dyspnea nor anoxemia. After a few days in the hospital the cyanosis clears up. To hasten the return of normal color, oxygen may be given and, in the more severe cases, methylene-blue can be administered intravenously. It has been recommended that the intravenous administration of methylene-blue in à dosage of 1 to 2 mg./kg. body weight will relieve cyanosis. Usually discontinuance of the home well water alone has proved to be sufficient. There is no established evidence that oxygen reduces methemoglobin in the blood and the use of oxygen is not recommended.

Cases herein reported were from southwestern Minnesota and Northwestern Iowa. Other physicians in southwestern Minnesota have seen additional cases and are familiar now with the danger. Likewise, farmers of the area refer to such babies as "blue-water babies" and are careful about what water is used.

I have since cared for seven similar cases of methemoglobinemia. One other is worthy of comment. A breast-fed infant, who was doing very well generally, showed moderate cyanosis of lips and finger tips and duskiness of the face within the first two weeks of returning to its farm home from the hospital. Recalling the case of the baby who showed cyanosis after drinking the milk of cows using contaminated farm well water, we instructed the mother to drink no more of the water from the farm well nor milk from cows which drank the same water. She reported later that the baby's color had cleared within the week and remained normal.

It would appear worthwhile to make blood analyses of the members of a household who drink these same waters, as well as nitrate and nitrite determinations on samples of breast milk and cow's milk. It is well known that many farm wells are shallow, poorly constructed and maintained, and a great number of them show contamination.

No cases of cyanosis in older infants and children have been reported.

Bacterial contamination is only presumptive evidence of the presence of toxic amounts of nitrate ion; it has been noted that toxic amounts of nitrates may exist in water which would be considered acceptable from the bacterial standpoint, and many heavily contaminated waters do not contain appreciable amounts of nitrate.

## Summary

Five cases of idiopathic cyanosis in babies are reported. They cleared and did not recur when well water used for drinking and formula was changed, as a result of demonstrated contamination with Coliform organisms.

These cases substantiate the contention of Comly that the toxic, or nitrate-containing water, is the cause of the cyanosis. This cyanosis appears as a result of the oxidation of hemoglobin into methemoglobin by the nitrites derived from nitrates present in the well water used for drinking or formula.

Cyanosis cleared within a few days following removal of the infant to the hospital, away from the home water supply, but recurred within one to two weeks after returning home to the use of the contaminated water.

One infant strongly suggested that milk from cows which drank the contaminated water may be the cause of moderate cyanosis when the milk supply is restricted to the single herd.

One infant suggested that cyanosis may occur in a breast-fed infant, if the mother drinks the contaminated well water, or the milk from cows drinking water from that well.

Many cases of cyanosis in early infancy in farm homes have been and still are being incorrectly treated for hypertrophy of the thymus gland.

Cyanosis in early infancy, occurring particularly in babies living on farms one to three weeks after birth, can be cleared by using uncontaminated water.

### References

1. Comly, H. H., Cyanosis in infants caused by nitrates in well water, J.A.M.A. **129**:112, 1945.
2. Schwartz, A. S., and Rector, E. J., Methemoglobinemia of unknown origin in a 2 week old infant, Am. J. Dis. Child. **60**:652, 1940.
3. Personal communication from U. S. Public Health Service, Washington, D.C.
4. Johnson, G., et al., Nitrate levels in water from rural Iowa wells, J. Iowa M. Soc. **36**:4, 1946.
5. Faucett, R. L., and Miller, H. C., Methemoglobinemia occurring in infants fed milk diluted with well water of high nitrate content, J. Pediat. **29**:593, 1946.
6. Ferrant, M., Methemoglobinemia; 2 cases in newborn infants caused by nitrates in well water, J. Pediat. **29**:585, 1946.
7. Medovy, H., Guest, W. C., and Victor, M., Water supply; cyanosis in infants in rural areas (well water methemoglobinemia), Canad. M.A.J. **56**:505, 1947.

### Spanish Abstract

**Cianosis en Infantes con Nitratos en el Agua para Beber como Causa**

Se han reportado siete casos en los cuales la cianosis idiopática o cianosis de etiología indeterminada que ha desaparecido al dejarle de dar al niño agua de pozo conteniendo un exceso de nitrados. Dos de estos infantes volvíeron a tenerla un poco dentro de una semana. En uno la cianosis desapareció cuando se le dejó de dar leche de vacas que bebían el agua, y el otro, que era niño alimentado al pecho, cuando la madre descontinuó el uso del agua y leche contaminadas.

De estos casos se deduce que la cianosis se puede desarrollar en infantes que beben agua o leche de vacas, o leche de madres que beben leche o agua que contienen cantidades excesivas de nitrados.

La cianosis que se debe a la metahemoglobinemia desaparecerá al quitarseles a los niños el uso de aguas que contienen nitrados. Se usó el oxígeno, pero sin ningún resultado. En casos severos de cianosis se recomienda la administración intravenosa de azul de metileno en dosis de 1 por 2 mg./kg. peso de cuerpo.

# PEDIATRIC ASPECTS OF HEMOPHILIA

*By* ARMAND J. QUICK, PH.D., M.D.
*Milwaukee, Wis.*

SINCE the pediatrician is often the first to detect hemophilia in a child, the problems presented by this condition are of special interest to him, and he knows how limited knowledge has been in the past concerning the basic nature of this disease. As the result of recent research, it is possible to formulate a simple and practical working hypothesis of the coagulation mechanism and to apply it directly to hemophilia.[1] This leads to a clearer understanding of the hemostatic defect in this disease, makes diagnosis more exact and treatment more effective and reliable.

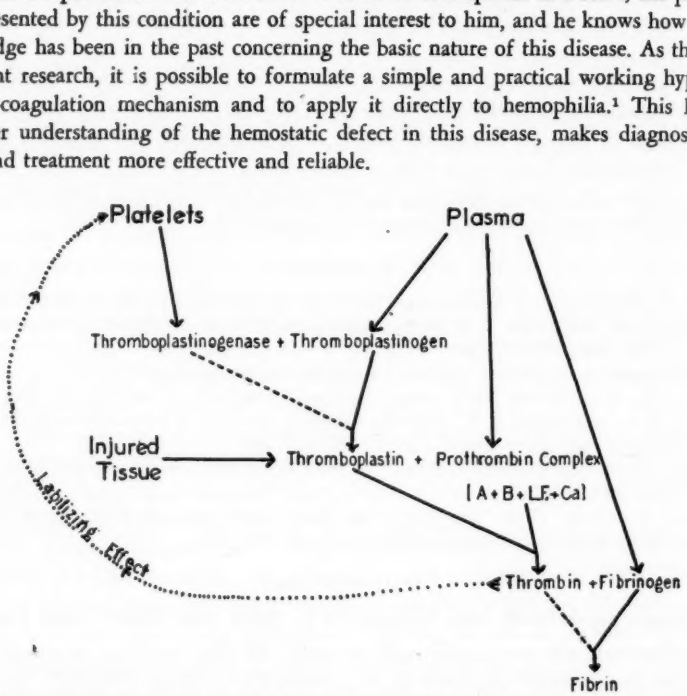


FIG. 1. The coagulation mechanism. The broken lines indicate catalytic or enzymatic action. The prothrombin complex consists of components A and B, the labile factor and bound calcium.

## THE COAGULATION DEFECT IN HEMOPHILIA

The coagulation mechanism can best be presented diagramatically, Fig. 1. Plasma, it will be observed, supplies all the known factors needed for the formation of thrombin except one which is derived from the platelets. The agent which the latter furnishes is not thromboplastin as is still commonly believed, but an enzyme which converts the

---

From the Department of Biochemistry, Marquette University School of Medicine, and Milwaukee Children's Hospital.

Presented before the Areal Meeting of the American Academy of Pediatrics, Milwaukee, June 29, 1948.

This investigation was supported in part by a research grant from the Division of Research Grants and Fellowships of the National Institute of Health, U. S. Public Health Service.

(Received for publication July 14, 1948.)

precursor of thromboplastin, thromboplastinogen, to the active form. The reaction between thromboplastin and the prothrombin complex has been found to be stoichiometric; therefore, the greater the amount of thromboplastinogen in the plasma the more prothrombin is converted and the more thrombin is formed. By means of a new procedure, the prothrombin consumption test, the thromboplastinogen can readily be estimated. In this test, blood is allowed to clot under specified conditions, and one hour later the prothrombin remaining in the serum is determined by the one-stage technic. In the coagulation of normal blood, from 60 to 90% of the prothrombin is consumed. In marked contrast nearly all the prothrombin remains unconverted when hemophilic blood coagulates. Only a small amount of thrombin is formed, but since this agent is an enzyme, it will eventually convert all of the fibrinogen to fibrin provided the reaction is confined to a small amount of blood in a test tube. The coagulability of hemophilic blood, therefore, appears greater than it actually is when functioning hemostatically under physiologic environments.

The immediate deficiency in hemophilia is thrombin. The cause of the poor production can readily be traced. Since the prothrombin time is normal, the prothrombin complex can be assumed to be quantitatively and qualitatively the same as in healthy blood. The defect must therefore be in the lack of available thromboplastin. Such a deficiency can result either from decreased thromboplastinogen or from defective platelets. The fact that washed hemophilic platelets, when added to normal deplateletized plasma, completely restore coagulability[2] clearly indicates that the platelets are not responsible for the lack of thromboplastin in hemophilia. The only remaining known factor to be considered is thromboplastinogen. All the available evidence strongly suggests that a deficiency of this factor is responsible for the bleeding tendency in hemophilia. As a result of the lack of thromboplastinogen, too little thrombin is formed to produce fibrin fast enough for effective hemostasis. In addition, another factor comes into play. Thrombin apparently labilizes platelets and this is an essential step in their lysis. The more thrombin, the faster the disintegration of platelets and, therefore, the speedier the formation of more thrombin. This establishes a chain reaction which in normal blood quickly gains momentum and completes coagulation in a few minutes. In hemophilic blood, the lack of thromboplastinogen keeps the chain reaction from being set in motion. The minute amount of thrombin is not enough to labilize the platelets and therefore they remain intact, which has been erroneously interpreted as an abnormal intrinsic stability. Both the lack of thrombin and the induced platelet stability undoubtedly share in causing defective hemostasis.

## The Diagnosis of Hemophilia

The impression one gains on reading standard text books is that the diagnosis of hemophilia is relatively simple and that it is readily made on the data of the occurrence of a bleeding tendency beginning early in life, a history of heredity and a prolonged coagulation time. To be sure, if a case offers this triad, the diagnosis is fairly evident, but even then it is not conclusive since hereditary hypoprothrombinemia may also exhibit these findings.[3,4]

The diagnosis of hemophilia can never be made unequivocally on clinical evidence alone, since the hemophilic type of bleeding can be simulated by other conditions notably by hypoprothrombinemia. Nevertheless, since hemophilia is by far the most common hemorrhagic disease in childhood, exclusive of the purpuras, any persistent bleeding

tendency should be tentatively considered hemophilia until proven otherwise. The hemophilic state is present from birth but often the disease is not diagnosed until the child is several years old. The main reason for this is that the baby is protected against trauma; and mild bleeding episodes such as resulting from circumcision and eruption of teeth are dismissed lightly especially if the coagulation time is reported to be normal.

TABLE I

THE PROTHROMBIN CONSUMPTION TIME IN A SERIES OF HEMOPHILICS

| Subject* | Age Years | Coagulation Time Lee-White, min. | Prothrombin Consumption, sec.** | Hereditary History |
|---|---|---|---|---|
| 1 | 31 | 28 | 9–10 | Positive |
| 2 | 11 | 210 | 10½ | " |
| 3 | 6 | 14 | 11 | " |
| 4 | 4 | 15½ | 10 | " |
| 5 | 37 | 37 | 10 | " |
| 6 | 3 | 20 | 11 | " |
| 7 | 9 | 10 | 9–12 | " |
| 8 | 16 | 16 | 25 | " |
| 9 | 24 | 9 | 10 | " |
| 10 | 7 | 7 | 12 | " |
| 11 | 5 | 7 | 17 | " |
| 12 | 6 | 14½ | 11 | Negative |
| 13 | 3 | 65 | 10–11 | " |
| 14 | 5 | 37 | 9–10 | " |
| 15 | 5 | 8 | 11 | " (?) |
| 16 | 11 | 7 | 9 | " |
| 17 | 7 | 30 | 10½ | " |
| 18 | 1½ | 45 | 10 | " |
| 19 | 17 | 9 | 16 | " |
| 20 | 13 | 33 | 10½–11 | " |
| 21 | 28 | 45 | 9–10 | " |
| 22 | 25 | 38 | 9–10 | " |
| 23 | 1½ | 45 | 11 | " |
| 24 | 1½ | 22 | 12 | " |

* Patients 3 and 4, 16 and 17, 21 and 22 are brothers.

** The prothrombin consumption test was performed as follows: Two ml. of blood were allowed to clot at 37° C. One hour after coagulation, the serum was removed and 0.1 ml. added to a mixture of 0.1 ml. fresh oxalated normal human plasma (treated with calcium phosphate), 0.1 ml. thromboplastin and 0.1 ml. of 0.02 M calcium chloride, and the coagulation accurately timed.

The diagnosis of hemophilia becomes almost certain when it is found that other male members of the family bleed, but in over one-third of the cases of hemophilia, inheritance cannot be established. It is very probable that in such cases the defect is transmitted silently through several generations of women, and one should therefore be cautious in applying the term sporadic. Since congenital hypoprothrombinemia is hereditary and by chance may present a hereditary pattern similar to hemophilia, it is obvious that laboratory studies must be the final means to make the diagnosis.

Of the laboratory methods employed for the diagnosis of hemophilia, the coagulation time is the oldest and the most widely used. This test is reliable only if done on venous blood under carefully standardized conditions.[5] Cognizance must be taken of the fact

that in very mild hemophilics, the coagulation time may be normal. The clotting time of recalcified plasma complements the Lee-White test and supplies additional information. The plasma obtained by high centrifugation of oxalated hemophilic blood will coagulate much slower than when obtained by slow centrifugation.[6] The coagulation time of normal recalcified plasma is little influenced by the speed of centrifugation. The only other condition in which this test gives the same results as in hemophilia is in congenital hypoprothrombinemia (deficiency of component A). The prothrombin time by the one-stage method readily differentiates hemophilia from the congenital types of hypoprothrombinemias.

The measurement of the prothrombin consumption promises to become the most reliable and useful test both for diagnosis and evaluation of therapy. Because of the deficiency of thromboplastinogen in hemophilic blood, only a trace of prothrombin is converted to thrombin and, therefore, the serum contains almost as much prothrombin as was originally present in the plasma. The prothrombin consumption time of serum obtained one hour after normal blood has coagulated is usually from 16 to 35 seconds, whereas hemophilic serum shows a range from 9 to 12 seconds. On examining Table I, one finds that in a series of 24 cases diagnosed as hemophilia, the prothrombin consumption test was in the latter range for all except three patients. These three had only a mild hemorrhagic tendency, but the hereditary history justified a diagnosis of hemophilia. No explanation for these findings can be offered, but it is hoped that means will develop to make the test more sensitive and thus detect faulty prothrombin activation in mild cases of hemophilia. The prothrombin consumption is also low in severe thrombocytopenic purpura, but in this disease the coagulation time is almost always normal, and the platelet count low, which makes its recognition relatively easy.

## Therapy

Hemophilia will most likely always remain an incurable disease, yet a defeatist attitude is never justified. Much can be done now in controlling the disease, and more effective measures will become available from the present basic advances.

The control of bleeding can be attempted locally or systemically, and the rationale of treatment becomes clear if one remembers the basic defect in hemophilia, which is the inadequate production of thrombin. Local treatment is directed to decrease the circulation of the injured area. The simplest way to accomplish this is by pressure and the application of cold. The vascular contraction which results brings about a slowing of the blood flow and a decrease in the blood pressure of the arterioles and minute arteries. Thrombin has a chance to accumulate; therefore, fibrin is formed and localized in the bleeding area and limited platelet agglutination occurs. This may be sufficient to abort a threatened hemorrhage. The application of heat on the contrary can convert a minor injury into a massive hemorrhage.

After the bleeding in a muscle or joint has subsided, heat should be cautiously applied to aid in the reabsorption of extravasated blood. This is best followed by diathermy, passive exercise, and light massage. Later active exercise should be encouraged to increase the circulation of the affected area in order to restore it to its normal state. Under such a regime ankyloses will be kept at a minimum.

Emergency operations on a hemophilic do not cause as much consternation as formerly. There is actual danger that the hazards of surgery may be underestimated, especially when the coagulation time is taken as the criterion of safety. A normal coagulation time

is no guarantee that the hemostatic efficiency has been sufficiently restored to meet the demands made by a major surgical procedure. Even the prothrombin consumption test, which is far more specific and quantitative, will require much more study and trial before its status as a measure of safety can be fully evaluated.

When an operation is necessary, the child should be given a transfusion preferably of fresh or lyophilized plasma. Whole blood may be used but since only the plasma supplies thromboplastinogen, twice as much volume must be given to achieve the same result. Good results have been reported following the use of plasma fraction I of Cohn.[7,8] Unfortunately this material is not generally available, and its effect has not been studied by the prothrombin consumption test. The transfusion should be given immediately before the operation and may be continued during the surgical procedure. The physiologic reason for this is that the transfusion will restore sufficient hemostatic power to the blood so that a fibrin plug will be formed in the lumen of the cut and torn arterioles and small arteries during the time in which they are in a state of contraction. This vascular contraction in response to injury is normal in hemophilia and usually lasts several hours. After relaxation sets in, hemostasis is much more difficult to achieve. That explains why it is easier to prevent hemophilic bleeding than to stop it and why the application of an ice bag often accomplishes more than pressure.

The management of a hemophilic patient requiring a major operation is illustrated by the following example: The patient, a boy five years old with a known history of hemophilia, developed the signs and symptoms of acute appendicitis. He was given 300 ml. of lyophilized plasma immediately before and during the operation. No excessive bleeding was encountered. The appendix was found normal, but a retroperitoneal hemorrhage behind the cecum was observed. The appendix was removed, all bleeding points ligated, and the wound closed. No further transfusion was given until 60 hours after the operation when he began bleeding into his incision. A summary of the findings are:

| | Lee-White Coagulation Time | Prothrombin Consumption Time (after 1 hour) |
|---|---|---|
| Before transfusion | 13½ min. | 11 sec. |
| Immediately after 300 ml. plasma | 3 min. | 21 sec. |
| Thirty-six hours postoperative | 7½ min. | 21 sec. |
| Sixty hours postoperative (bleeding into incision) | | 11 sec. |
| Immediately after 250 ml. fresh blood | | 25 sec. |
| Twenty-four hours after transfusion | 5½ min. | 19 sec. |

Not all cases respond as well to therapy as the one presented. Infection complicates the situation, and the extraction of an abscessed tooth may cause more trouble than a clean major operation. There are still too many unknown factors to permit treating the problems arising in hemophilia lightly. Bleeding can occur which neither transfusion nor the administration of any plasma protein fraction will control.

Last but not least to be mentioned in therapy is the physician's task to encourage the parents of hemophilic children. Fathers and mothers should never be told the condition is hopeless. Many hemophilics are living useful and productive lives. Some have successful professional careers. Many hemophilics can cope with their physical handicaps, and a wise physician can prevent them from becoming mental cripples.

## Summary

The bleeding tendency in hemophilia is due to a congenital and hereditary lack of thromboplastinogen which causes an incomplete conversion of prothrombin and an insufficient production of thrombin. The diagnosis should be based on the correlation of clinical data, history of heredity and the results of certain laboratory tests, of which the coagulation time, the clotting time of recalcified plasma, the prothrombin time and the prothrombin consumption time are most significant. Important in therapy are: first, protection against injury; second, local and systemic measures to stop bleeding; and third, the preparation of the hemophilic patient for an emergency operation.


## References


1. Quick, A. J., Studies on the enigma of hemostatic dysfunction of hemophilia, Am. J. M. Sc. **214**:272, 1947.
2. Quick, A. J., and Stefanini, M., Activation of plasma thromboplastinogen and evidence of inhibitor, Proc. Soc. Exp. Biol. and Med. **67**:11, 1948.
3. Quick, A. J., Congenital hypoprothrombinaemia and pseudo-hypoprothrombinaemia, Lancet **2**:379, 1947.
4. Quick, A. J., Components of prothrombin complex, Am. J. Physiol. **151**:63, 1947.
5. Quick, A. J., Honorato, R. C., and Stefanini, M., Value and limitations of the coagulation time in the study of the hemorrhagic diseases, Blood **3**:1120, 1948.
6. Quick, A. J., Diagnosis of hemophilia, Am. J. M. Sc. **201**:469, 1941.
7. Lewis, J. H., Tagnon, H. J., Davidson, C. S., Minot, G. R., and Taylor, F. H. L., Relation of certain fractions of the plasma globulin to the coagulation defect in hemophilia, Blood **1**:166, 1946.
8. Wright, C. S., Doan, C. A., Dodd, V. A., and Thomas, J. D., Hemophilia: current theories and successful medical management in traumatic and surgical crises, J. Lab. and Clin. Med. **33**:768, 1948.


## Spanish Abstract

### Aspectos Pediatricos de la Hemofilia


El defecto básico en la hemofilia es la producción inadecuada de la trombina debida a la falta congénita de tromboplástinogeno, como se ha encontrado en estudios recientes. Se puede calcular el tromboplástigeno que existe en el plasma por medio de un nuevo análisis que mide la protombina consumida en la coagulación. Este análisis sirve como uno de los medios más específicos que existen ahora para diagnosticar la hemofilia. El tiempo de coagulación puede ser algunas veces engañoso. La historia clinica y records de herencia son importantes. Al niño hemofílico se le debe proteger de daños. Cuando haya derrame de sangre, hay que aplicar presión y frío immediatamente. Si esto no da resultado, entonces se recomiendan transfusiones de plasma o de sangre fresca. En caso de operación de mergencia el paciente debe recibir primero plasma a sangre y se debe determinar el efecto por el análisis d consumo de protrombina, para así ver la necesidad de subsecuentes transfusiones.


*561 N. 15th St.*

# IMMUNOHEMATOLOGIC OBSERVATIONS ON ERYTHROBLASTOTIC INFANTS. I. DIAGNOSIS AND PROGNOSIS

*By* PHILLIP STURGEON, M.D.
*Los Angeles, Calif.*

MOST reports on the Rh factor have been concerned with the genetic aspects of the factor, the therapy of patients with erythroblastosis, and the detection of Rh antibody in the mother's serum. The serologic aspects of the erythroblastotic infant's red cells and serum have received relatively little attention.[1-10]

This study was undertaken to evaluate available practical immunohematologic procedures which, when performed in the first few hours of life, might establish the diagnosis of erythroblastosis and give a reliable prognosis. The need for a specific and reliable test has become increasingly important, especially for the pediatricians who must consider the need of exchange transfusion therapy. To be most effective, transfusion should be started during the first few hours of life.[11, 12]

The present report deals with quantitative immunologic studies in 26 consecutive, suspected erythroblastotic infants.

## MATERIAL

Eleven samples of sera and red blood cells from infants in the maternity wards of various hospitals in the city were brought to this hospital for study (Cases 1-4, 12, 16, 18, 21-24). Observations were made on 15 infants admitted to the hospital, in whom erythroblastosis was suspected clinically (Cases 5-11, 13-15, 17, 19, 20, 25, 26). The two groups include several infants in whom the differential diagnosis of jaundice or anemia became necessary in the first few weeks of life (Cases 17-26).

The provisional diagnoses (sometimes erroneous) were based on prenatal antibody titers performed elsewhere by AB serum or agglutination technics and/or by the clinical and cytohematologic data available in the first few days of the infant's life. Titrations of the maternal sera were not carried out in advance in this laboratory; from that standpoint, therefore, each case was approached as an unknown.

Clinical data on infants that were not admitted to the hospital were furnished by the attending pediatricians. Those admitted to the hospital had, in addition to the immunologic investigation, the following tests: icterus index, van den Bergh, cephalin flocculation, and electroencephalogram. The data from these latter studies are not included in their entirety in this report.

## METHODS

A direct developing test[9] (Coomb's test) was performed on each blood sample and the strength of the reaction noted. (See Figure 1.) In the performance of the direct developing test, a rigid routine was followed in order that subsequently noted reactions could be reliably compared. A few drops of whole blood were added to a 100 mm. x 13 mm. test tube, and it was filled to within 1 cm. of the top with 0.9% saline. The tube was inverted several times to insure adequate mixture and immediately centrifuged at high speed; the supernatant was then poured or aspirated off as completely as possible. The tube was again filled with saline, the remaining cells dispersed by shaking and inverting, and the suspension centrifuged immediately for the second time. The process was repeated for the third time, after which the remaining cells were suspended in saline to an approximate suspension of 2 to 5% by volume. Complete removal of the supernatant saline of each wash-

From the Pathology Department of Childrens Hospital, Los Angeles, and the Department of Pediatrics, University of Southern California School of Medicine.

(Received for publication July 9, 1948.)

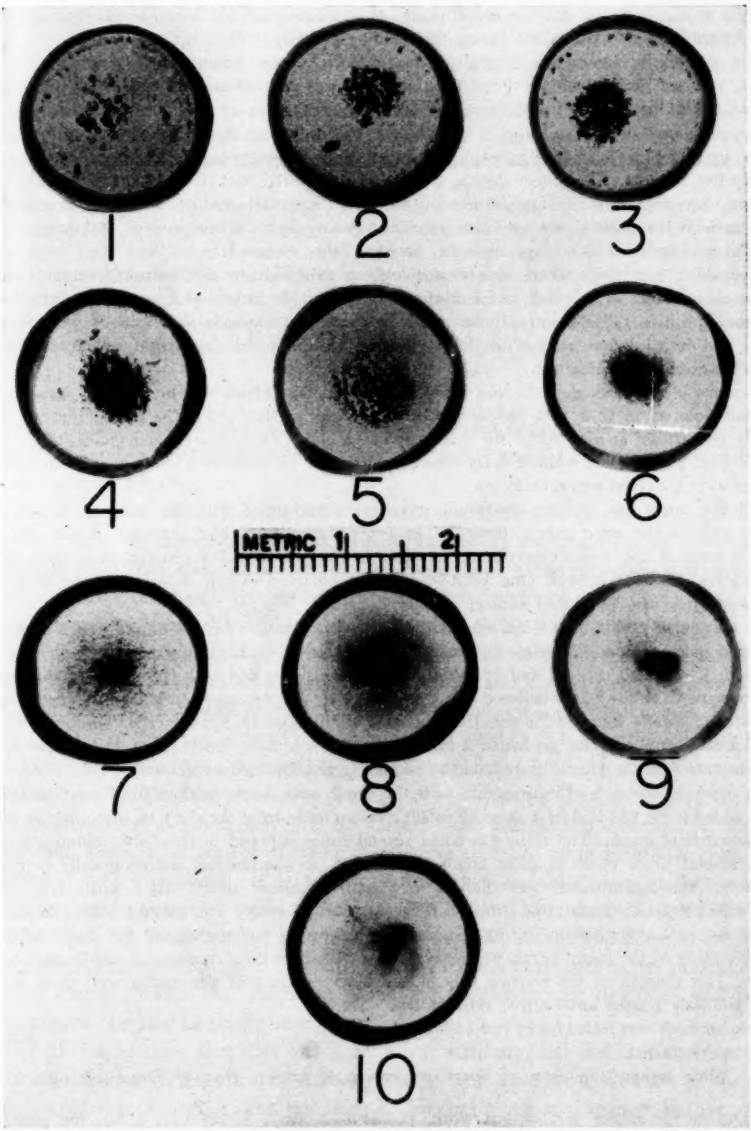


FIG. I. Direct Development Test. Strength of Reaction: 1-3 Positive, strong. 4-6 Positive, moderate. 7-9 Positive, weak. 10 Negative.

ing was considered important to reduce to a minimum neutralization of the developing serum antibodies by the residual plasma proteins. At the same time, delay and excessive washing was avoided in order to minimize the decrease in the degree of sensitization of the infant's cells from the elution of their antibody into the saline during the washing process.

The developing serum was lyophilized to protect its titer. Approximately every two to three weeks, a 1 ml. sample of the lyophilized material was reconstituted to volume to serve as undiluted stock; the reagent for the test was always freshly prepared in a 1/10 dilution from some of the undiluted stock. One drop of the fresh 1/10 developing serum was then added on a slide to an equal-size drop of freshly washed unknown cells. These were mixed and allowed to stand exactly five minutes. To prevent drying, the slide was covered with a moistened petri dish; before reading, the slide was tilted and turned 20 times. The actual reading was done at exactly five minutes with the unaided eye against a good background light. When positive, the strength of the reaction was recorded as strong, moderate, or weak. (See Figure I.)

If positive, the baby's serum was titrated for free antibodies by the indirect developing technic. In the performance of this test, serial dilutions of the infant's unknown serum were incubated with known D-positive cells. From each test tube in the series, the cells so sensitized were then prepared and tested individually with the developing serum by the same rigid technic as described under the direct developing test.

A saline eluate from the cells was made and titrated. The eluate was prepared by incubating for one-half hour at 56°C. a 50% suspension of the infant's washed cells. The preparation was immediately centrifuged at high speed for three minutes and the rather heavily hemoglobin-tinged supernatant fluid pipetted off without delay. Serial dilutions of the unknown eluate were then made and titrated as in the above serum titrations.

All the direct and indirect developing tests were performed with the same antihuman rabbit serum and by the same technic described in a previous report.[9] Not included in that report are further tests of the reagent performed by Drs. G. Jorgensen and P. Strong on a series of 100 consecutive newborn infants. One positive test was obtained, which occurred in the only infant in their series who developed clinical erythroblastosis.[35]

In the above titrations, 0.5 ml. of unknown serum or eluate in serial dilutions was mixed with an equal quantity of a 2% saline suspension of fresh, group-O, D-positive and D-negative cells. In Cases 2, 3, 4, 8, 10, 11, 14, and 15, all titrations were performed with fresh cells of the probable Rh genotype CDe/cde.* It is believed that these cells were appropriate because, being D-heterozygous, they should closely simulate the sensitivity of most erythroblastotic infants' cells. The serial dilutions were made using separate graduated 1-ml. pipettes. In addition, observations for the presence of "agglutinins"† in the eluates were made by inspecting the RBC sedimentation patterns.

In order to compare older methods with the above tests, "autoconglutination" was investigated on a slide by the addition of a drop of infant's cells (settle from the clot) to an equal-size drop of the supernatant serum. The slide was tilted several times, allowed to stand five minutes, and then tilted several times more. If gross clumping occurred, it was checked microscopically to rule out rouleaux. Auto-agglutination was checked in a similar manner except that a small drop of cells was added to a relatively large drop of saline instead of serum. The infant's cells also were observed for auto-agglutination during the washing process in preparation for the direct developing test. Blocking of the infant's cells was determined by typing with a commercial anti-D agglutinating serum. The strength of the reaction was judged by comparison of the results with those obtained from similarly treated unsensitized cells of type CDe/cde.

Free antibody was tested for by two additional methods:

1. Serum methods.

A. "Slide technic": a drop of heavy suspension of known group-O D-positive cells in their

* During the earlier part of this work, (Cases 1, 5, 6, 7, 9, 12, 13), it was not possible to know the probable genotype of the test cells. The author is further indebted to Drs. G. Jorgensen and P. Strong for the differential Rh type determinations.

† As used in this study, the term "agglutinin" refers to an antibody that causes clumping of specific red cells in physiologic saline. In contrast, the term "blocking antibody" (conglutinin), refers to an antibody that cannot cause clumping in saline but which will clump specific red cells when both are suspended in a system of approximately 7% or more protein.

serum was added to a drop of infant's serum on a slide, allowed to stand five minutes, tilted, and read.

B. "Test tube technic": a 2% suspension of group-O D-positive cells in AB serum was mixed with equal parts of infant's serum, incubated one-half hour, and observed for gross sedimentation pattern; centrifuged, tapped gently, and read for clumping; then examined microscopically.

2. Saline methods.

A. Agglutination: 2% D-positive cells in saline were mixed with equal quantities of serial saline dilutions of infant's serum, incubated one hour, and observed for gross sedimentation pattern only.

B. This preparation was then washed three times and used for completion of the indirect developing titrations.

When indicated, follow-up observations were made by one or all of the above methods. If the pediatrician elected to perform an exchange transfusion, most of the above observations were made on the "first" and "last" blood withdrawn and repeated in from one to seven days. Results of these follow-up observations will be published in a subsequent report. In Cases 1, 5, 16, where there was marked discrepancy between the reported prenatal maternal antibody titers and the subsequent tests and clinical observations, postpartum maternal serum was titrated by the indirect developing technic, by ordinary saline agglutination, and by the AB serum technic.

## Results

Table I summarizes the pertinent data obtained from consecutive infants who were suspected of having erythroblastosis on clinical grounds and/or by reason of results of prenatal maternal Rh titrations.

From the data in Table I, it becomes apparent that only one of the tests, the direct developing test, demonstrated perfect correlation with the presence or absence of erythroblastosis (final clinical or pathologic diagnosis). However, the correlation of any of the above tests with the severity of the disease was not as perfect. In general, cases which gave a weak developing test and were negative to all other tests were very mild or subclinical (Cases, 3, 4, 5). Most of the moderate to severe cases, as judged clinically, including instances of icterus gravis, hydrops, and kernicterus, gave a moderate developing test, had an eluate titer of 1/16 or more, showed some evidence of blocking, and had a titer of free antibody of 1/8 or greater. Cases 13, 14, 15, clinically the most severe erythroblastotis, gave strong direct developing tests; in contrast, however, Cases 13 and 14 showed no free antibody, the cells typed strongly D-positive, and the titer of the saline eluate was relatively low. In Case 14 the postpartum maternal serum was titrated two weeks later by the indirect developing technic, using CDe/cde cells, and a titer of 1/512 was found. It is felt, therefore, that the cells used in that infant's serum and eluate titrations were appropriate. Hill and Haberman[6] observed that Rh antibodies have not been demonstrated by the eluate technic except when free in the serum of the infant. This observation has been confirmed for the most part in the present study except in Cases 13 and 14. "Autoconglutination" by the technic described was found in two out of the five clinically severe cases (Cases 13 and 14).

Table II summarizes the data in three cases with prenatal indications considered sufficient for exchange transfusion. Although at present complete evaluation of the need for exchange transfusion is not possible, it has been advised against in our clinic, irrespective of past history and prenatal titers, in cases showing all of the following three phenomena: 1) a negative or weak positive direct developing test, 2) a positive reaction with anti-D agglutinating serum, and 3) an absence of free antibody in the baby's serum by the indirect developing technic (see Cases 1, 3, 4, 5, 16).

In Cases 1, 5, 16, the decision to carry out exchange transfusion had been reached

TABLE I

SUMMARY OF IMMUNOLOGIC AND CLINICAL DATA FROM SUSPECTED ERYTHROBLASTOTICS

| Case | Age[1] | Sensitization of infants' red cells | | | | | | Titre free antibody infants' serum | | | | Severity of Disease and Clinical Remarks |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | Direct developing | Autoconglutination | Autoagglutination | D typing (blocking) | Eluate titer | | Agglutination | AB serum | | Developing | |
| | | | | | | agglutination | developing | | slide | test tube | | |
| 1 | 6 hr. | neg. | neg. | neg. | pos. weak | neg. | neg. | neg. | neg. | neg. | neg. | No clinical evidence of erythroblastosis. Congenital atelectasis. No hepatosplenomegaly, anemia, or icterus. Expired. |
| 2 | 96 hr. | neg. | neg. | neg. | pos. strong | — | — | — | neg. | — | — | Undiagnosed. Anemic. Jaundiced. No maternal antibodies demonstrated by serum, developing, or saline technic. Survived. |
| 3 | 0 | pos. weak | neg. | | pos. strong | — | — | neg. | neg. | neg. | neg. | Subclinical: questionably prolonged "physiologic jaundice." Survived. |
| 4 | 0 | pos. weak | neg. | neg. | pos. mod. | — | — | neg. | neg. | neg. | neg. | Subclinical: slightly prolonged physiologic jaundice. Survived. |
| 5 | 48 hr. | pos. weak | neg. | neg. | pos. strong | — | — | neg. | — | — | neg. | Mild: jaundice at 48 hours. 2 small transfusuons at 10 days. Survived. |
| 6 | 2 hr. | pos. mod. | neg. | neg. | pos. mod. | neg. | neg. | neg. | neg. | neg. | 1/8 | Moderate: no jaundice splenomegaly, or hepatomegaly. Hgb. 10.4 gm. Exsanguination transfusion, 230 ml. Benign course. Survived. |
| 7 | 96 hr. | pos. mod. | neg. | neg. | pos. weak | neg. | 1/32 | neg. | neg. | neg. | 1/8 | Moderate: jaundice slow to clear; 35 ml. transfusion 4th day. Return 10 days later for 100 ml. transfusion. Survived. |
| 8 | 24 hr. | pos. mod. | neg. | neg. | pos. strong | — | — | neg. | neg. | neg. | 1/8 | Moderate: icterus started in first 24 hr. Hgb. 12 gm. Exsanguination transfusion, 367 ml. Survived. |
| 9 | 48 hr. | pos. mod. | neg. | neg. | neg. | neg. | 1/32 | neg. | neg. | neg. | 1/2 | Moderate: mild icterus; mod. anemia. 4 transfusions of 60–120 ml. in course of 20 days. Survived. |
| 10 | 36 hr. | pos. mod. | neg. | neg. | pos. strong | neg. | 1/16 | neg. | neg. | neg. | 1/16 | Moderate: icterus developed at 36 hrs. Exsanguination transfusion 190 ml. Survived. |
| 11 | 96 hr. | pos. mod. | neg. | neg. | pos. mod. | — | — | neg. | — | — | 1/16 | Severe: mod. icterus and anemia. Clinical kernicterus. Exsanguination transfusion 365 ml. Continues opisthotonic. Survived. |
| 12 | 0 | pos. mod. | neg. | neg. | pos. mod. | neg. | 1/16 | neg. | neg. | neg. | 1/8 | Severe: hydrops developed within first hour. Expired. |
| 13 | 96 hr. | pos. strong | pos. | neg. | neg. | neg. | 1/128 | neg. | neg. | 1/2 | 1/32 | Severe: icterus gravis. Exsanguination transfusion, 260 ml.; 2 subsequent transfusions. Prolonged course. Survived. |
| 14 | 10 hr. | pos. strong | pos. | neg. | pos. strong | neg. | 1/4 | neg. | neg. | neg. | neg. | Severe: icterus gravis. Hgb. 6.5 gm. Liver and spleen palpable. Exsanguination transfusion. Infarction of bowel. Expired |
| 15 | 0 | pos. strong | neg. | neg. | pos. strong | neg. | 1/4 | neg. | neg. | neg. | neg. | Severe: slight icterus; liver and spleen palpable. Scrotum edematous. Exsanguination transfusion. During proceeding, expired. |

[1] 0 = Cord blood.

on the basis of past obstetric history and prenatal antibody titers obtained from outside laboratories. All three of these cases had high and/or rising titers demonstrated by "AB serum" technic. Two of the three pregnancies had been interrupted because of these findings. The material in Cases 1 and 16 was made available a few hours after birth, when the severity of the erythroblastosis could not be predicted on a clinical basis. Table II summarizes reported prenatal data, observations on the infant's blood, and follow-up titrations on the mother's serum.

In all three cases, exchange transfusion was contemplated but withheld on the basis of findings in the infant's blood by the developing technics. These data are not submitted for a comparison between the specificity of the developing and other technics for the detection of maternal Rh antibody, but primarily to show the practical value

TABLE II

THREE CASES WITH PRENATAL INDICATIONS CONSIDERED SUFFICIENT FOR EXCHANGE TRANSFUSION

| Case | History | Laboratory Data* | Course | Direct Developing | Maternal antibody 2 wk. postpartum† |
|---|---|---|---|---|---|
| 1 | Primigravid. I. M. injection of blood or serum in childhood. | Mother RH−, Father Rh+. Maternal titer: 1/640 8½ mo. by AB serum technic. | Induced 1 week early. Rh+. No jaundice or anemia. Respirations weak; cyanotic. Expired 48 hours. Pathologic Dx: congenital atelectasis. | Negative | Agglutination, negative. Conglutination, negative. Developing, negative. |
| 5 | Gravid II; Para I Previous child stillborn, 6th month. | Mother RH−, Father Rh+. Maternal titer: 6–8th mo., 1/512; 8th mo. 1/16,000, AB serum. 1/256 agglutination. | Cesarean section 8th month. Rh+. Jaundice began at 48 hrs. Slight anemia. 35 ml. transfusion second day and at end of 10 days. Mild course. | Positive weak | Agglutinaion, 1/256 Conglutination, 1/1024 Developing, 1/32 ? |
| 16 | Gravid III; Para II. Stillborns at 7 & 8 mo.; latter, macerated fetus | Mother RH−, Father RH? Maternal titers: 4th mo., 1/1024; 7½ mo., 1/4096; at term 1/1024. AB serum technic. | Term, spontaneous delivery. Rh−. No jaundice. No anemia. Normal child. | Negative | Agglutination, negative. Conglutination, negative. Developing negative. |

* Reported from elsewhere.
† Done in author's laboratory.

of studies on the newborn infant's blood before the final decision regarding the type of therapy is reached. The benign appearance of such cases in the first few hours serves only to intensify the anxiety of the pediatrician who, in an attempt to weigh the relative values of expectant observation versus transfusion therapy, must resort to inconclusive observations such as hemoglobin determinations, differential counts, and clinical signs of icterus. The results of the direct developing test in addition to the clinical condition of each of these patients (1, 5, 16) placed the balance in favor of instituting no therapy in spite of past history and prenatal titers. The decisions were well justified by subsequent clinical developments.

Table III presents results of the developing test in instances of jaundiced, anemic, or otherwise suspected erythroblastotic infants where information was inadequate to make the diagnosis of erythroblastosis. It briefly summarizes the available data and illustrates instances in which the direct developing test may prove of decisive value in the differential diagnosis of jaundice and anemia in the neonatal period.

TABLE III

USE OF THE DIRECT DEVELOPING TEST IN THE DIFFERENTIAL DIAGNOSIS OF JAUNDICE AND ANEMIA IN THE NEONATAL PERIOD

| Case | Age on coming under observation | Indication for performing direct developing test | Result of test | Subsequent clinical course—diagnosis |
|---|---|---|---|---|
| 17* | 2 weeks | Jaundiced; entered hospital with diagnosis of sclerema secondary to septicemia. Parents not available for blood typing. No obstetric history available. | Positive, moderate. | Blood cultures negative. Expired. Dx: erythroblastosis. Secondary sclerema. |
| 18 | 2 days | Jaundice starting at 36–48 hours. Third child. No previous history suggestive of erythroblastosis. | Negative | Normal neonatal. Jaundice mild; cleared up on 5th day. Dx: physiologic jaundice. |
| 19 | 11 days | Jaundice developed in 24 hours. No anemia; stools pale. First pregnancy. | Negative. | Jaundice increased; No anemia. Cephalin flocculation negative. Dx: suspected bile duct atresia. |
| 20 | 4 weeks | Jaundice developed gradually since birth. No anemia. Stool yellow. | Negative. | Jaundice subsided. No anemia. Cephalin flocculation 4+. Dx: hepatitis, unknown etiol. |
| 21 | 0 | Hydropic. Not jaundiced. Two previous normal children. No prenatal antibody titration. Mother B, D+. Father O, D+. | Negative. | Expired following exsanguination transfusion. Gross pathology inconsistent with erythroblastosis. 6 weeks postpartum, no maternal antibodies demonstrable by AB serum or developing technic using father's cells. Dx: undiagnosed. |
| 22 | 1 day | Normal appearing infant. No anemia. 1 previous miscarriage. Mother D−. No prenatal titrations. | Negative. | Normal neonatal. Dx: normal child. |
| 23 | 1 day | Normal appearing infant. Pediatrician told, when child 1 day old, that mother had rising titer of Rh antibodies. | Negative. | Normal neonatal. Dx: normal child. |
| 24 | 6 weeks | Anemic (Hgb. 10 gm.). No prenatal Rh data available. | Suggestive positive microscopically. | Given one transfusuon, has remained well 4 months. Dx: probable erythroblastosis. |
| 25 | 10 days | Anemic (5.6 gm.) Large spleen and liver. Mother D−, father D+. No neonatal history available. | Positive, moderate. | Free antibody 1/4 by indirect technic. Transfused. Dx: erythroblastosis; congenital anemia. |
| 26 | 10 days | Anemia (Hgb. 10 gm.) Data on parents? | Positive, moderate. | Dx: erythroblastosis; congenital anemia |

* It is of interest to note as in case #17 that sclerema has complicated several of our cases of erythroblastosis.

## DISCUSSION

Hill and Haberman[6] state regarding the value of the specificity of the developing technic, "if this specificity can be completely established in routine use this test appears to be of utmost practical value for diagnosis, prognosis and treatment." Cases of erythroblastosis referred to this hospital are frequently not accompanied by important data regarding maternal titers, Rh type, and past obstetric history. Hence, a simple test like the direct developing test with a specificity for both diagnosis and prognosis certainly would be of the utmost practical value. At present the data, although somewhat

limited,* indicate that the developing test originally described by Coombs, Mourant, and Race[3] has such a specificity. There remains the problem of establishing its value for routine use. To date this has not been possible because a stable, potent, standard developing serum is not widely available.

Based on the cases observed thus far, qualitative differences in the strength of the developing reaction in our hands correlated closely with the subsequently observed clinical severity of the disease. Thus, it has been possible to give a relatively accurate prognosis. The following qualitative direct developing reactions seem to justify the anticipation of the indicated severity of the disease:

| Direct Developing | Severity of Disease |
|---|---|
| 1) Negative: | Rh sensitized erythrocytes are not present |
| 2) Positive, weak: | Subclinical to mild |
| 3) Positive, moderate to strong: | Moderate to severe, including kernicterus, severe icterus gravis, and hydrops |

In the third category it is possible that observations made on blood taken immediately postpartum would yield results which correlate more closely with clinical findings than observations made at random from birth to four days of age. Separation of the moderate cases of icterus gravis from the more severe and fatal ones, including cases of hydrops, is most desirable. This was not accomplished with the technics employed.

A quantitative method for estimation of the severity of a case of erythroblastosis was not uncovered. The indirect developing titer of free antibody in the infant's serum in general gives rough quantitative data that correlate directly with the clinical course of the disease. A titer of 1/8 or more in most instances was accompanied by a severe clinical course. In two instances (Case 14 and 15), however, the relationship did not hold. Possibly closer correlation could be obtained with the use of one of the concentrated albumin technics.[13, 14] The indirect developing test showed free antibody in eight out of 12 cases; in contrast, the AB serum technic gave a positive result only once, which was a severe case.

Sensitization of the infant's red cells as shown by methods other than the direct developing test were of value only when results were positive, as follows:

| Positive Test | Severity of Disease |
|---|---|
| 1) Blocked cells: | "Moderate" to "severe" |
| 2) "Autoconglutination" | Positive in 2 of 5 "severe" cases |
| 3) Developing titer of saline eluate of 1/128 | "Severe" |

* Subsequent to the original preparation of this manuscript, developing tests have been performed on the red cells of 85 additional, untreated, neonatal infants suspected of having erythroblastosis. Forty positive and 45 negative reactions occurred. No significant evidence of a false positive nor a false negative result has been found.

In the few cases giving a positive result in which clinical erythroblastosis was not definitely apparent in two to three days, maternal antibody titers were reported as positive and the case in question represented a second or later pregnancy. In these instances the developing test was weak.

In cases clinically resembling severe erythroblastosis but giving negative developing tests, Rh subgroups have been determined on the mother's and father's and/or infant's red cells. The maternal serum was then tested for Rh antibody with red cells of the appropriate genotype. In none of these instances has maternal Rh antibody been demonstrated.

Any or all of these phenomena were absent in moderate to severe cases; none of the above tests was positive in mild to negative cases. A more sensitive modification for "autoconglutination" may be possible by suspension of the infant's cells in concentrated albumin, adult serum, whole blood, or gelatin[5, 13, 14] instead of in the infant's serum as was done in this study. To date, however, none of these technics has been reported to possess the specificity for diagnosis shown by the direct developing test. These modified technics could prove of further value in the estimation of prognosis.

Auto-agglutination and free agglutinins were not demonstrated on any infant's cells or in any infant's serum. Likewise, eluates made from sensitized red cells failed in all instances to show the presence of agglutinins. Frequently high titers of incomplete antibodies were found by the developing technic. Possibly, agglutinins would have been found had the sensitized cells been centrifuged before washing rather than read by sedimentation pattern only. On the other hand, agglutination was looked for during the washing process (after centrifugation) in saline solutions of less than 50% serum; thus false agglutination due to "conglutination" was avoided.[14] Haberman and Hill[7] and Carter and Loughrey,[2] using a similar technic, reported their liberating agglutinins from the erythroblastotic infant's washed red cells. Wheeler and Scholl,[10] also using an eluate technic, were able to demonstrate incomplete antibodies in 10 out of 11 cases of erythroblastosis; however, in no case did their saline eluate give an observable agglutination.

## Conclusions

With the use of the described developing test and other technics in immunohematologic observations on red blood cells and sera from untreated neonatal infants suspected of having erythroblastosis, it has been possible to make a specific diagnosis and to obtain data which will contribute to a more accurate prognosis than has been possible heretofore.

The AB serum, saline, and blocking tests as described lack the specificity and sensitivity of the direct developing tests for diagnosis; but when used alone, if the results are positive, they are of some value in the estimation of prognosis.

## References

1. Wiener, A. S., Conglutination test for Rh sensitization, J. Lab. & Clin. Med. **30**:662, 1945.
2. Carter, B. B., and Loughrey, J., Method of demonstrating anti-Rh agglutinins in cases of erythroblastosis fetalis, Am. J. Clin. Path. **15**:575, 1945.
3. Coombs, R. R. A., Mourant, A. E., and Race, R. R., Detection of weak and "incomplete" Rh agglutinins; new test, Lancet **2**:15, 1945.
4. Coombs, R. R. A., Mourant, A. E., and Race, R. R., Invivo isosensitization of red cells in babies with hemolytic disease, Lancet **250**:264, 1946.
5. Abelson, N. M., cited by Potter, Edith L., Rh: Its Relation to Congenital Hemolytic Disease and to Intragroup Transfusion Reactions, Year Book Publishers, Inc., Chicago, 1947, p. 294.
6. Hill, J. M., and Haberman, S., Demonstration of Rh antibodies in newborn and further evidence of pathogenesis of erythroblastosis, J. Lab. & Clin. Med. **31**:1053, 1946.
7. Haberman, S., and Hill, J. M., Clinical significance of Rh factor, Texas State J. Med. **40**:182, 1944.
8. Bloxsom, A., Outlook for infants receiving anti-Rh agglutinins from isoimmunization of mothers, Texas State J. Med. **42**:279, 1946.
9. Sturgeon, P., New antibody in serum of patients with acquired hemolytic anemia, Science **106**:293, 1947.

10. Wheeler, W. E., and Scholl, Mary Louise L., Determination of anti-Rh antibody in infants with erythroblastosis fetalis, Am. J. Dis. Child. **74**:274, 1947.
11. Platou, E. S., Heilig, W. R., Bergan, R., and Tudor, R. B., Exchange transfusion; new method of treatment for erythroblastosis fetalis, Journal Lancet **67**:180, 1947.
12. Wallerstein, R., Substitution transfusion, new treatment for severe erythroblastosis fetalis, Am. J. Dis. Child. **73**:19, 1947.
13. Diamond, L. K., and Denton, R. L., Rh agglutination in various media with particular reference to value of albumin, J. Lab. & Clin. Med. **30**:821, 1945.
14. Wiener, A. S., Hurst, Jane G., and Sonn-Gordon, Eve B., Studies on conglutination reaction, with special reference to nature of conglutinin, J. Exp. Med. **86**:267, 1947.
15. Jorgesen, G., and Strong, P., Personal communication.

SPANISH ABSTRACT

## Observaciones Inmunohematologicas en Infantes Eritroblastoticos. I. Diagnosis y Prognosis

Se hizo una prueba para avaluar los procedimientos adaptables al estudio de la sangre de cordon, el cual puede establecer la diagnosis de eritroblastosis y dar una prognosis segura.

Se estudiaron veintiseis infantes que se creía tenían eritroblastosis. Se hizo un análisis de desarrollo directo (análisis de Coomb) en las células rojas de cada infante. Además se titularon los sueros de varios infantes por medio de la técnica de desarrollo indirecta para el anticuerpo libre, y se hicieron elutriaciones salinas de las células rojas de estos infantes. Los descubrimientos hechos por medio de esta técnica forman contraste con los resultados obtenidos par medio de técnicas más viejas y se hizo una correlación de los informes de arriba con cursos clínicos subsecuentes.

Solamente el análisis de desarrollo directo demostró correlatión perfecta con la presencia o ausencia de eritroblastosis. También hubo una correlación regular entre la fuerza de la reacción de desarrollo y el curso clínico subsecuente.

Se presentan tres casos con indicaciones prenatales consideradas suficientes para asegurar el cambio de transfusión; en cada caso se tomó una decisión de no hacer este procedimiento a causa de la reacción de desarrollo débil o negativa. Subsecuente curso clínico justificó estas decisiones.

El análisis de desarrollo puede ser de valor decisivo en diagnosis diferenciales de ictericia y niños neonatales anémicos.

*4614 Sunset Blvd.*

# SUCCESSFUL REMOVAL OF HEMANGIOMA OF THE LIVER IN AN INFANT

*By* THURMAN SHULLER, M.D., JOSEPH L. ROSENZWEIG, M.D., AND JAMES B. AREY, M.D.
*New Orleans, La.*

THE rarity with which one encounters clinically recognizable hemangiomas of the liver in infancy prompts us to report the successful surgical removal of such a tumor from an infant 22 days of age.

Benign hemangiomas occur more frequently in the liver than in any other internal organ.[1, 2, 3] Among 570 hemangiomas studied by Geschickter and Keasbey,[1] 109 were located in the liver. Although they rarely produce symptoms,[3, 4] Shumacker[2] in 1942 was able to collect reports of 66 patients with hemangiomas of the liver for which operation was performed, and added a case of his own. The tumors were removed surgically from 56 patients, the youngest being six years old. At least four reports of surgical removal of hemangiomas of the liver have appeared since that time.[5–8]

Although rare, hemangiomas of the liver occurring in infants have been previously reported by a number of authors.[9–12] To our knowledge, however, the case we are reporting is the first in which a hemangioma of the liver has been successfully removed from an infant.

## CASE REPORT

E. C., a first-born white male, was admitted to the Tulane Pediatric Service when he was 15 days old. The mother's pregnancy apparently had been entirely normal and delivery was spontaneous at term. Although the baby was slightly cyanotic for a few moments immediately after birth he was easily resuscitated and no further cyanotic episodes occurred. He was fed a standard formula and his course seemed uneventful until the eighth day of life. At that time the mother felt a mass in the abdomen "about the size of a baseball." On the ninth day the patient was fretful, spit up or vomited about half of his feedings, and his temperature rose to 38.3°C.; a physician made a diagnosis of acute pharyngitis, hospitalized the baby and gave parenteral penicillin for four days, after which all symptoms subsided and the infant seemed well. However, the mass was apparently increasing in size so the baby was brought to Charity Hospital of Louisiana for further study.

At the time of admission the infant looked well; he weighed 3.8 kg. and his temperature was 37.7°C. There was questionable injection of the pharyngeal mucosa and a rather typical heat-rash. There was no visible tumor mass, the abdomen was soft, and normal peristaltic sounds were audible over the left side of the abdomen. On the right side of the abdomen, however, there was palpable a firm, smooth, rounded mass which was not tender. It occupied the entire right upper quadrant, extended laterally beyond the mid-axillary line and inferiorly to a level three centimeters below the umbilicus. The inferior border felt somewhat sharp and the consistency of the mass was thought to be that of liver. The left lobe of the liver was palpable just below the costal margin in its usual position. There was no thrill, bruit, nor distention of superficial abdominal veins over the mass.

---

From the Departments of Pediatrics and Pathology, Tulane University School of Medicine, and the Charity Hospital of Louisiana at New Orleans.

The portion of this study carried out in the Department of Pathology has been supported in part by a grant from the United States Public Health Service.

(Received for publication August 7, 1948.)

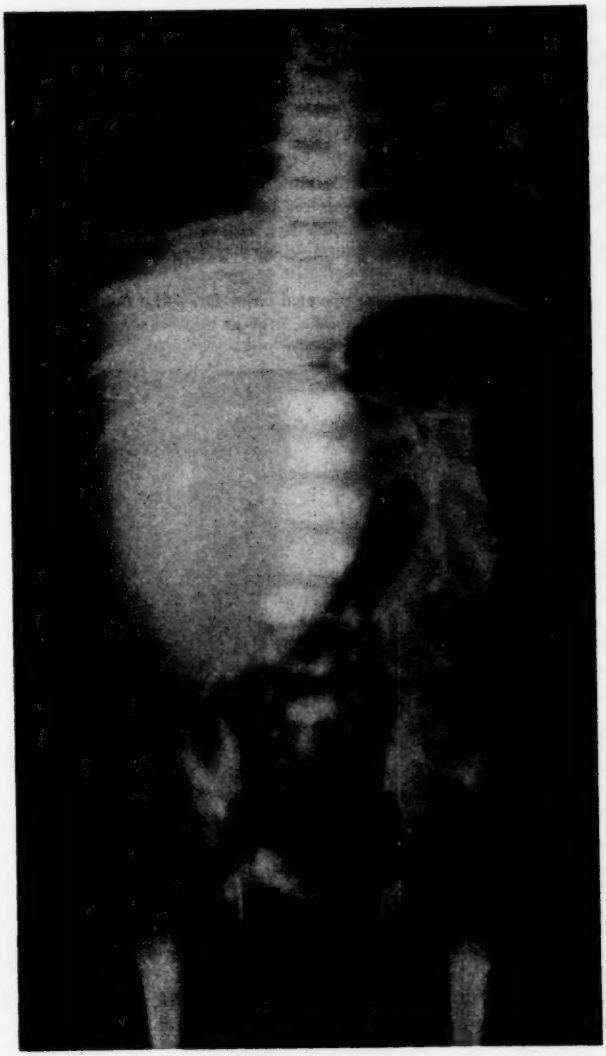

FIG. 1. Flatplate of the abdomen showing a soft tissue density occupying the right upper quadrant and displacing the ascending colon, hepatic flexure, and part of the transverse colon inferiorly and to the left.

Routine urinalysis was negative. Hgb. was 13 gm./100 cc. blood, RBC 4.6 million/cmm., and WBC 15.25/cmm. with 57% polynuclear cells, 35% lymphocytes, 6% monocytes, and 2% eosinophiles. ESR was 7 mm. in one hour (Wintrobe) and the hematocrit 39 mm. Clotting time was six minutes, bleeding time 1½ minutes, and prothrombin time was 56% of normal. Serologic tests for syphilis were negative. Serum bilirubin was 0.25 mg./100cc. at the 1 minute direct reading and

0.55 mg./100cc. at the 15 minute total determination. Thymol turbidity was 2.0 units, cephalin flocculation was zero. Serum alkaline phosphatase was 3.83 Bodansky units, serum calcium was 10.8 mg./100 cc., and serum phosphorus was 5.27 mg./100 cc. Roentgenograms of the chest and long bones showed no abnormalities. A flat plate of the abdomen revealed a soft tissue density occupying the right upper quadrant and displacing the ascending colon, hepatic flexure, and part of the transverse colon inferiorly and to the left (Fig. 1). Intravenous pyelograms indicated that the kidneys were in normal position and excreted dye satisfactorily.

The patient took and retained a standard formula. Vitamin K was given parenterally. He received three transfusions of whole blood—90 cc. (24 cc./kg.), 60 cc. (16 cc./kg.), and 40 cc. (10 cc./kg.)—on the 3rd, 4th and 6th hospital days. Following these transfusions the hemoglobin was 15 gm., bleeding time 1½ minutes, clotting time 1½ minutes, and the prothrombin time was still 56% of normal.

On the 22nd day of life the patient was operated on by Dr. Alton Ochsner. A transverse incision was made and on entering the peritoneal cavity a large globular tumor mass was encountered. The

FIG. 2. Hemangioma of the liver showing varying sized spaces lined by endothelial cells. (x 170)

broad base of this tumor was attached to the anterior border of the lower half of the right lobe of the liver just lateral to the gall bladder. This mass, together with a rim of normal liver tissue, was excised; bleeding was controlled by the use of mattress sutures and "gelfoam." The liver bed was drained through a separate stab incision. The patient received 100 cc. (26 cc./kg.) of blood during the operation.

Immediately following surgery the patient's condition seemed good; two hours later the hemoglobin level was 9.0 gm./100 cc. He received two transfusions of blood totaling 110 cc. (29 cc./kg.) within the next 10 hours, after which the hemoglobin level remained above 12 gm. Eighteen hours postoperatively his temperature suddenly rose to 39°C., but subsided rapidly following symptomatic measures. It was felt that this febrile episode represented a reaction to pyrogens received with the transfusion; blood matching was rechecked and no incompatibilities could be demonstrated. Penicillin was given intramuscularly during the first six days postoperatively while the drain was in place; low grade fever disappeared when this was removed. Only parenteral fluids were given for the first 24 hours postoperatively, then small oral feedings were begun, gradually increased and well tolerated. The patient received parenteral vitamin B complex, vitamin C and vitamin K daily until full feedings were attained on the 7th day. He was discharged on the 18th day; at that time he weighed 4.3 kg., a gain of 0.5 kg.

When last seen, six months after surgery, the infant was entirely well and weighed 8.2 kg.; his wound was well healed and careful examination revealed no abnormalities.

*Pathologic examination:* The specimen consisted of a roughly discoid piece of tissue measuring 8 x 5 x 4.2 cm. One surface was coarsely granular and presented several irregular pitted areas up to 1.5 x 0.4 cm. This surface was covered by a thin fibrous membrane and varied from grey to purplish red. The opposite surface of the specimen was covered by a very thin layer of brownish hepatic tissue; this surface apparently represented the area of resection.

On hemisection the mass varied from a shiny translucent yellowish grey to a deep purplish red. It was firm and somewhat elastic and appeared to be covered everywhere by a very thin greyish capsule. At the line of junction with hepatic parenchyma this capsule was barely visible, but the line of junction was distinct and was marked by numerous slit-like spaces resembling dilated veins. Within the tumor proper, however, no such spaces were visible, the substance being homogenous in consistence although varied in color.

Histologic sections stained with hemotoxylin and cosin revealed a well circumscribed but poorly encapsulated tumor composed of innumerable empty spaces varying from approximately 20 micra in diameter to large cystic spaces roughly 2 x 1 mm. (Fig. 2). The spaces varied considerably in outline, the smaller ones tending to be circular or slightly elongated, whereas the larger ones were extremely irregular; this irregularity was produced by numerous finger-like projections which appeared to represent tributary vessels communicating with larger spaces or vessels. The spaces were lined by flattened or somewhat cuboidal cells composed of vesicular or small dark nuclei with little or no demonstrable cytoplasm. A few spaces contained precipitated serum or red blood cells, and a few of the larger spaces contained thrombi with beginning organization.

The stroma between the aforementioned endothelial lined spaces was scanty and consisted of a loose fibrillar tissue containing fibroblasts and vesicular nuclei indistinguishable from those of the endothelial cells lining the vascular spaces. A few condensed bands of collagen were present and there were a few small foci of hematopoietic cells as well as a rare small bile duct; otherwise recognizable hepatic tissue was not present within the tumor proper.

A considerable number of small bile ducts were present within the incomplete connective tissue capsule, otherwise the hepatic tissue about the tumor showed no abnormalities. There was no evidence of compression or atrophy of the hepatic cords. In one area the tumor extended to but not through the capsule of the liver.

The pathologic diagnosis was benign mixed capillary and cavernous hemangioma of the liver.

## Comment

As with most benign hemangiomas of the liver previously reported, an accurate preoperative diagnosis was not made. In about half of those reported,[2] the only presenting complaint was a "silent" upper abdominal mass. Others had variable pains or sensations of heaviness in the epigastrium, anorexia, eructation, nausea or postprandial distress.

A mass in the right upper quadrant with roentgenograms demonstrating displacement of the colon downward and to the left suggested that there was a tumor mass attached to the right lobe of the liver.[13, 14] Primary or metastatic malignancy, hemangioma, and hamartoma were all considered as possibilities, but it appeared impossible to differentiate these preoperatively. Calcification of the tumor, such as may be demonstrated occasionally in hemangiomas of the liver pathologically[15] or roentgenologically[7, 16] was not present in this case. A preliminary punch biopsy was suggested but was not considered advisable because of the hazard of severe or uncontrollable hemorrhage and death.[17–19] We believed a more reasonable course to be early exploration and excision.

Favorable response of hemangiomas of the liver to X-ray therapy has been reported,[20, 21] but the treatment of choice is complete excision. The possibility of continued enlargement of the tumor with resultant pressure symptoms, the possibility of malignancy and the very real danger of spontaneous rupture[9–11, 22] make early surgical treatment advisable.

SUMMARY

A large solitary benign hemangioma of the liver was successfully removed from an infant 22 days old.

REFERENCES

1. Geschickter, C. F., and Keasbey, L. E., Tumors of blood vessels, Am. J. Cancer **23**:568, 1935.
2. Shumacker, H. B., Jr., Hemangioma of liver; discussion of symptomatology and report of patient treated by operation, Surgery **11**:209, 1942.
3. Ewing, J., Neoplastic diseases: Treatise on Tumors, 4th Ed., W. B. Saunders Co., 1940, Philadelphia, p. 249.
4. Watson, W. L., and McCarthy, W. D., Blood and lymph vessel tumors, Surg., Gynec. & Obst. **71**:569, 1940.
5. Morton, H. B., Large pedunculated cavernous hemangioma of liver, Am. J. Surg. **56**:673, 1942.
6. Peale, A. R., and Coombs, J. N., Large hemangioma of liver, successfully removed surgically, Am. J. Clin. Path. **16**:792, 1946.
7. Pickrell, K. L., and Clay, R. C., Lobectomy of liver, Arch. Surg. **48**:267, 1944.
8. Ayres Netto, P., and Amorim, J., Hemangioma cavernoso do lobo esquerdo do figado, Rev. de cir. de São Paulo **8**:257, 1942.
9. Hendrick, J. G., Hemangioma of liver causing death in newborn infant, J. Pediat. **32**:309, 1948.
10. Kissinger, C. C., Sternfeld, E., and Zuker, S. D., Rupture of cavernous hemangioma as cause of death in newborn infant, Ohio State M. J. **36**:383, 1940.
11. Hammer, F., Beiträge zur Pathologie des Neugeborenen; Leberangiom beim Neugeborenen, Ztschr. f. Geburts. u. Gynäkol. **50**:223, 1903.
12. Steffen, A., Ueber Angiom der Leber, Jahrb. f. Kinderh. **19**:348, 1883.
13. Hofmann, C., Ueber wahre Cysten der Leber mit besonderer Berücksichtigung der klinisch bedeutungsvollen Cystadenome, Mitt. a.d. Grenzgeb. d. Med. u. Chir. **10**:476, 1902.
14. Stoesser, A. V., and Wangensteen, O. H., Solitary nonparasitic cysts of liver, Am. J. Dis. Child. **38**:241, 1929.
15. Cripps, H., Large naevoid tumor removed from liver, Brit. M. J. **2**:18, 1903.
16. Aspray, M., Calcified hemangiomas of liver, Am. J. Roentgenol. **53**:446, 1945.
17. Tokushige, Y., Über einen Fall vom bösartigen Hämangioma cavernosum der Leber, Taiwan Igakkai Zassi **39**:2050, 1940.
18. M'Weeney, E. J., Enormous angeioma of liver, J. Path. & Bact. **16**:401, 1911.
19. Mantle, A., Unusually large angeioma of liver, Brit. M. J. **1**:365, 1903.
20. Ray, B. S., Large, cavernous hemangiomata of liver; report of an inoperable case treated with roentgenotherapy, Ann. Surg. **109**:373, 1939.
21. Morris, J. H., Hemangioma of liver; successful resection of left lobe, Ann. Surg. **111**:147, 1940.
22. Chiari, Kongress der Deutschen Gesellschaft für Geburtshilfe und Gynäkologie, München. med. Wchnschr. **56**:1615, 1909.

SPANISH ABSTRACT

## La Extraccion Quirurgica de un Hemangioma del Higado

La extracción quirúrgica de un hemangioma benigno del higado, llevada a cabo con buen exito en un niño de 22 días de edad, es reportada. Los autores citan cincuenta y siete casos similares anteriormente reportados, teniendo el paciente más joven seis anos de edad.

El dato importante fue la presencia de una masa "silenciosa" en la parte superior del abdomen, no revelando los datos de laboratorio anormalidades importantes. Estudios roentgenográficos mostraron una masa en el quadrante superior derecho, que desplazabael colon hacia abajo y hacia la izquierda. El diagnóstico quedó confirmado unicamente después del estudio histológico.

La imposibilidad de hacer un diagnóstico seguro pre-operatorio, más indudables peligros asociados al retardo en el tratamiento, hacen que los autores advoquentemprana exploración y extirpacion de tales tumores.

*1430 Tulane Ave.*

# COMBINED IMMUNIZATION AGAINST DIPHTHERIA, TETANUS AND PERTUSSIS IN NEWBORN INFANTS

## III. Relationship of Age to Antibody Production

*By* PAUL A. DI SANT'AGNESE, M.D.
*New York, N.Y.*

REPORTS in the literature on the influence of age on antibody production were briefly reviewed on a previous occasion.[1] It was concluded that experimental work has shown that immunologic processes of the newborn animal are not identical with those of older individuals of the same species. The production of antibodies in response to an antigenic stimulus in newborn animals does not correspond qualitatively nor quantitatively to that of the fully mature animal. The validity of applying these conclusions to the human newborn infant has been questioned in recent years.[2]

In this report, we aim to evaluate the effect of increasing age on antibody response to antigenic stimuli through a comparison of the results of prophylactic inoculation in newborn infants and in a group of older children.

In all instances the same triple combined antigen ("Alhydrox") was used, and following the same routine. The only difference was in the age at which the inoculations were administered. One group (designated Series X in the present report) was injected in the newborn period. Three injections of the triple combined antigen were given at intervals of four weeks. The first dose was administered at the age of one week, the second at the age of five weeks, and third at nine weeks of age. The results were evaluated by determination of serum levels of antibacterial and antitoxic antibodies. The findings have been reported in detail in previous reports.[1, 3]

The "older" children (referred to hereafter as Series B) received the first prophylactic inoculation after the age of three months, in most cases between the ages of six months and one year. The other two injections were given at intervals of four weeks from the first. The results of antibody determinations one month and six months after third injection have been reported previously.[4] Antibody titrations done one year after completion of inoculations and after administration of a booster dose are presented for the first time. It is realized that the term "older" children may be misleading in view of the young age of the majority of the patients in Series B. However, for the sake of simplicity the term "older" children will be used.

The material used for immunization, the schedule of inoculation, the laboratory methods employed and the serum antibody levels considered "protective" have been discussed elsewhere.[1, 4]

In addition to evaluating the effect of increasing age on antibody response to antigenic

From the Department of Pediatrics, Columbia University, the Babies Hospital, Vanderbilt Clinic and the Sloane Hospital.

Supported by a grant from Cutter Laboratories, Berkeley, Calif.

Submitted in partial fulfillment of the requirements for the degree of Doctor of Medical Science, College of Physicians and Surgeons, Columbia University.

(Received for publication July 6, 1948.)

stimuli, this paper will include a comparison between the two age groups in regard to local and systemic reactions to prophylactic inoculation.

## Reactions to Prophylactic Inoculation

Some observations can be made on the incidence of systemic reactions resulting from administration of the vaccine to newborn infants (Series X) as compared with older

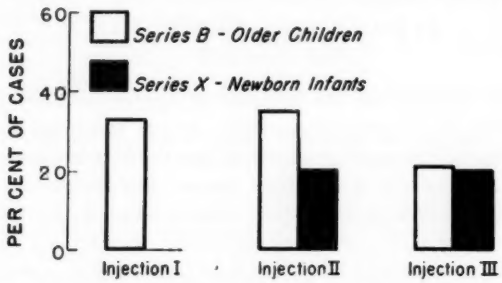


Fig. 1. Proportion of patients with fever 37.8°-40°C. following injections of triple combined antigen.

children (Series B).[1, 4] The incidence and severity of these reactions increased with subsequent injections in newborns, while the reverse was true of the "older" children. In Figure 1 this is shown in the case of fever (37.8°-40°C.). In response to the first injection no elevations of temperature were observed among the newborn infants (Series

TABLE I

Comparison of Tetanus Antitoxin Titers Achieved by Newborn Infants (Series X) and Older Children (Series B)

| Tetanus antitoxin titers | Time after completion of inoculations | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | One Mo. | | 4 to 6 Mo. | | 10 to 14 Mo. | | 10 to 30 days after booster dose | |
| | X | B | X | B | X | B | X | B |
| Without protective titer* | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| With protective titer | 100% | 100% | 100% | 100% | 100% | 100% | 100% | 100% |
| Total cases | 128 | 82 | 110 | 80 | 63 | 27 | 30 | 19 |
| With high titer† | 92% | 95% | 83% | 91% | 73% | 67% | 97% | 95% |

* "Protective" antitoxin titers—0.1 unit/cc. or more.
† "High" antitoxin titers—>1.0 unit/cc.

X) in contrast with an incidence of 33% in the "older" children (Series B). After the second injection the number of patients with fever was still considerably smaller in Series X as compared with Series B. After the third injection almost no difference existed between the two groups.

This behavior may be explained by the lack of general reactivity characteristics of

newborn infants. With increasing age, febrile responses to infectious stimuli become more common.

Local reactions did not follow the pattern of the systemic reactions. Only slight variance was evident in the incidence and severity of erythema and infiltration in the two

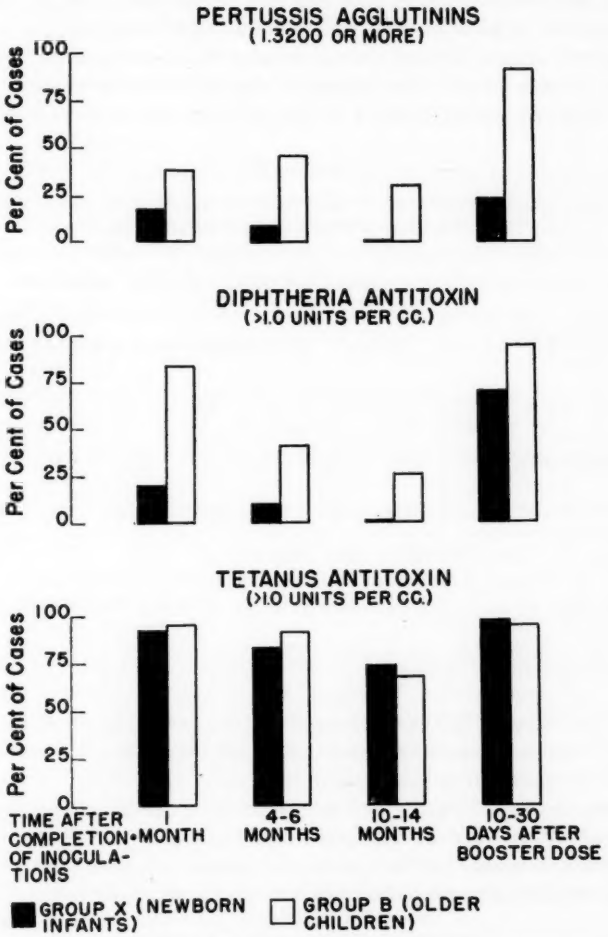


FIG. 2. Comparison of "high" antibody titers achieved by newborn infants (Series X) and "older" children (Series B)

groups.[1, 4] However five sterile abscesses were observed in the newborns, none in the "older" children, a difference which is difficult to explain. Different lots of the triple combined antigen may have been responsible for these findings.

### TITRATION OF TETANUS ANTITOXIN

Results of titration of tetanus antitoxin in Series X and Series B appear in Table I.

In the year following completion of the immunizing injections all patients tested in both Series X (newborn infants) and B ("older" children) had "protective" tetanus antitoxin titers (0.1 unit/cc. or more).

As for "high" tetanus antitoxin titers (>1.0 unit/cc.), one month after the third prophylactic injection 92% of Series X and 95% of Series B had such antitoxin levels. A steady decrease in the number of patients with "high" antibody titers was observed with the passage of time. Four to six months after the inoculations the decline in antitoxin levels was more marked in the newborns than in the "older" children. At this time only 83% of patients tested in Series X had antitoxin titers of more than 1.0 unit/cc.

TABLE II

COMPARISON OF DIPHTHERIA ANTITOXIN TITERS ACHIEVED BY NEWBORN INFANTS (SERIES X) AND OLDER CHILDREN (SERIES B)

| Diphtheria antitoxin titers | Time after completion of inoculations | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | One Mo. | | 4 to 6 Mo. | | 10 to 14 Mo. | | 10 to 30 days after booster dose | |
| | X | B | X | B | X | B | X | B |
| Without protective titer* | 15% | 1% | 28% | 0 | 23% | 15% | 0 | 0 |
| With protective titer | 85% | 99% | 70% | 100% | 77% | 85% | 100% | 100% |
| Total cases | 123 | 82 | 103 | 80 | 57 | 27 | 29 | 19 |
| With high titer† | 20% | 84% | 12% | 41% | 0.5% | 26% | 70% | 95% |

* "Protective" antitoxin titer—0.03 unit/cc. or more.
† "High" antitoxin titers—>1.0 unit/cc.

as against 91% in Series B. Ten to 14 months after injection the percentage of children with "high" tetanus antitoxin titers was not significantly different in the two groups, 73% for Series X and 67% for Series B.

Both groups responded equally well to booster dose, administered to both B and X cases 10 to 14 months after the third prophylactic injection.

The similarity in tetanus antitoxin production between infants injected in the newborn period (X) and several months after birth (B) is seen in Figure 2.

## TITRATION OF DIPHTHERIA ANTITOXIN

Titration of the serum levels of diphtheria antitoxin are reported in Table II. Table III summarizes the results of statistical comparison of the numbers of children in the two series with "protective" and "high" diphtheria antitoxin titers.

One month after the third inoculation 85% of newborn infants (X) and 99% of "older" children (B) had diphtheria antitoxin titers of 0.03 units/cc. or more ("protective" titer). The difference between the two groups is significant statistically. When tested again, four to six months after the third injection, the difference between the two series of patients had increased. At that time, the percentage of newborns (X) with

"protective" antitoxin titers had declined to 70%, while all the "older" children were "protected." By 10 to 14 months after the injections there had been a decline from 100 to 85% in the number of children with diphtheria antitoxin titers of 0.03 unit/cc. or more in Series B, while no further decrease was observed in Series X. The difference between the two age groups at this time was not significant statistically and presumably due to chance distribution (Table III). Ten to 30 days after booster dose, administered one year after completion of the immunizing injections, 100% of patients in both series had "protective" diphtheria antitoxin levels.

The "high" diphtheria antitoxin titers (> 1.0 unit/cc.) achieved after inoculation are represented in Figure 2.

A very significant difference was observed one month after completion of the three injections between the number of newborns (X) who achieved "high" diphtheria antitoxin titers (20%) and of "older" children (B) with such antibody levels (84%). In both groups the "high" diphtheria antitoxin titers declined steadily thereafter as seen in Figure 2. Upon retesting four to six months and 10 to 14 months after inoculation, a significant difference persisted between the two series. The "older" children (B) consistently showed a greater percentage of "high" diphtheria antitoxin titers than the newborn infants (X).

After booster dose the percentage of newborns with antitoxin titers of more than 1.0 unit/cc., rose to 70% as against 95% for the "older" children (Fig. 2). This difference is not significant statistically and could have been due to sampling error (Table III).

### Titration of Pertussis Agglutinins

In Table IV are summarized the results of titration of serum pertussis agglutinins. In Table V are recorded the results of a comparison by statistical methods of the pertussis agglutinin titers achieved after the three immunizing injections in the two series of cases.

One month after the third injection a very significant difference was present in the two groups in the percentage of cases with "protective" pertussis agglutinin titers: 54% in Series X; 86% in Series B. Upon retesting three months later (four to six months after inoculations) the difference between the two series of cases was even greater. The percentage of "protected" children at this time dropped to 33% in Series X, while there was virtually no change in the figure for Series B (82%). In the following six months the situation was reversed, there being a marked decline in pertussis antibody titers to 50% in Series B, no change in Series X (34%). Ten to 14 months after the injections, the difference in the numbers of patients in the two groups with titers of 1:400 or higher was not statistically significant (Table V).

After booster dose, about one year after the third prophylactic injection, there was a marked increase in the percentage of "protective" titers to 63% in Series X and 92% in Series B. Because of the small number of patients tested at this time the difference between the two groups of cases cannot be considered within the limits of statistical significance (Table V).

The percentage of cases with "high" pertussis agglutinin titers in Series X and Series B are compared in Figure 2.

A significant difference existed one month after completion of the three immunizing inoculations in the percentage of cases with agglutinin titers of 1:3200 or higher between

TABLE III

RESULTS OF STATISTICAL COMPARISON OF DIPHTHERIA ANTITOXIN TITERS ACHIEVED BY NEWBORN INFANTS (SERIES X) AND OLDER CHILDREN (SERIES B)

| Time after completion of inoculations | Cases with protective titers | | Cases with high titers | |
|---|---|---|---|---|
| | $\chi^2$* | P | $\chi^2$ | P |
| 1 month | 9.67 | 0.0019 | 78.2 | $\ll$0.0001 |
| 4–6 months | 23.1 | $\ll$0.0001 | 18.1 | $<$0.0001 |
| 10–14 months | 0.31 | 0.5755 | 9.78 | 0.0018 |
| 10–30 days after booster dose | — | — | 3.19 | 0.0740 |

* In this table and in Table V, when the value for $\chi^2$ is between 3.84 and 6.64, the difference between the two age groups will be considered of "borderline significance." Values for $\chi^2$ of 6.64 or greater will be considered "statistically significant." Values for P (probability) are also given for each comparison.

TABLE IV

COMPARISON OF PERTUSSIS AGGLUTININ TITERS ACHIEVED BY NEWBORN INFANTS (SERIES X) AND OLDER CHILDREN (SERIES B)

| Pertussis agglutinin titers | Time after completion of inoculations | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | One Mo. | | 4 to 6 Mo. | | 10 to 14 Mo. | | 10 to 30 days after booster dose | |
| | X | B | X | B | X | B | X | B |
| Without protective titer* | 46% | 14% | 67% | 18% | 66% | 50% | 37% | 8% |
| With protective titer | 54% | 86% | 33% | 82% | 34% | 50% | 63% | 92% |
| Total cases | 125 | 82 | 108 | 80 | 47 | 26 | 30 | 12 |
| With high titer† | 17% | 38% | 9% | 46% | 0.5% | 31% | 23% | 92% |

* "Protective" agglutinin titer—1:400 or higher.
† "High" agglutinin titers—1:3200 or higher.

TABLE V

RESULTS OF STATISTICAL COMPARISON OF PERTUSSIS AGGLUTININ TITERS ACHIEVED BY NEWBORN INFANTS (SERIES X) AND OLDER CHILDREN (SERIES B)

| Time after completion of inoculations | Case with protective titers | | Cases with high titers | |
|---|---|---|---|---|
| | $\chi^2$ | P | $\chi^2$ | P |
| 1 month | 20.0 | $\ll$0.0001 | 10.5 | 0.0012 |
| 4–6 months | 42.8 | $\ll$0.0001 | 31.5 | $\ll$0.0001 |
| 10–14 months | 1.18 | 0.2757 | 10.2 | 0.0014 |
| 10–30 days after booster dose | 2.12 | 0.1450 | 13.7 | 0.0002 |

Series X (17%) and Series B (38%). This difference was even more pronounced four to six months after the injections. Only 9% of newborns had "high" titers at this time against 46% in the "older" group. Similar findings were obtained upon retesting 10 to 14 months after inoculation.

Ten to 30 days after booster a marked increase in pertussis antibody levels was noted in both series. The increase was much more marked in the "older" group (92%) than in newborn infants (23%). The difference between the two groups, despite the small number of patients, was highly significant statistically (Table V).

## Discussion

1. *Effect of Age on Antibody Production:* A great difference existed in the levels of pertussis agglutinins achieved after prophylactic injections by a group of newborn infants (X) as compared with a group of "older" children (B) (Tables IV and V Figure 2). The patients in the older age group consistently (even after booster dose) showed higher pertussis agglutinin titers when tested at various intervals after completion of prophylactic inoculations. No passive immunity against whooping cough (serum agglutinins) was present at birth in the infants under investigation.[1] The poorer results in the younger age group as compared with the "older" children, after injection of equal amounts of the same immunizing material and following the same schedule, must therefore be attributed solely to immaturity of the immune mechanisms which prevented full "sensitization" of antibody-forming tissues in the younger infants.

On the other hand, tetanus antitoxin production following active immunization (Table I, Figure 2) was equally good in infants injected in the newborn period (Series X) and in those who received their prophylactic inoculations several months after birth (Series B). How can this be explained in view of the foregoing claim that poor antibody response following pertussis immunization was due to immaturity of antibody-producing mechanisms? The immunizing agent used in the present investigation ("Alhydrox"), as we have stated, contains tetanus toxoid of unusually high antigenic capacity. It may be reasonably assumed on the basis of the results following tetanus inoculation that, if a sufficiently great antigenic stimulus is given, the handicap due to immune-mechanism immaturity may be overcome and satisfactory immunization achieved.

These conclusions are further emphasized by the results of inoculation against diphtheria. "Older" children (Tables II and III, Figure 2) produced higher diphtheria antitoxin titers after injection than the infants inoculated in the newborn period. After administration of a booster dose, however, the difference in antitoxin levels between the two groups was not significant. It must therefore be assumed that the degree of immunization against diphtheria achieved by both age groups was comparable. The relatively poor initial showing of the newborn infants may be attributed at least partly to the presence of trans-placentally acquired diphtheria antitoxin.[3] Here again the powerful antigenic stimulus afforded by a total of 75 Lf of diphtheria toxoid was potent enough to overcome the combined handicaps of tissue immaturity and existing passive immunity to diphtheria.

The conclusion that antibody-response to an antigenic stimulus increases with advancing age confirms in humans the experimental evidence obtained by other authors in animals.[1] We cannot fully agree with Sako[2] that age makes no difference in immune response to prophylactic inoculation. Another more cautious conclusion is that while the results of immunization in the very young infant may not be as good as in the older

child a significant degree of protection against clinical infections may be obtained by starting prophylactic injections in the newborn period. In this respect our conclusion that the immunologic handicap due to tissue immaturity can be overcome in many instances by increasing the antigenic stimulus is especially important.

When does maturation of immune mechanisms take place? Evidence can be gathered from the literature and from our own results[4] that the critical period of immune tissue immaturity is in the first few weeks after birth. The difference in antibody response to booster doses at six months and a year of age in infants immunized in the newborn period[3] points to the fact, however, that full immunologic maturation does not take place for at least several months.

One more effect of age on antibody production should be pointed out. Diphtheria and tetanus antitoxin levels and pertussis agglutinin titers (Tables I, II and IV) decreased more readily in infants injected in the newborn period (Series X) than in the "older" children (Series B).

2. *Limitations of the Present Investigation:* Some of the limitations of this investigation should be mentioned. First, the group of so-called "older" children whose antibody response to inoculation was compared with that of newborn infants, were children over the age of three months, mainly between six months and one year of age. We have presented evidence[3] in a discussion of antibody production following re-injection, that the immune mechanisms at six months of age are still relatively immature. If the age of this control series of cases had been greater the difference in antibody levels between the two age groups might have been more marked.

Evaluation of the results of the three basic inoculations in newborn infants was based on antibody titrations carried out one month after administration of the third immunizing injection. The antibody levels achieved represented the composite result of three injections of vaccine given at intervals of four weeks. It is quite possible that in some instances the antibody-producing tissues of the newborns were too immature to react to the first injection administered at the age of one week. Success in tissue-sensitization in these cases may have followed only the second or third injection, given at five and nine weeks after birth respectively.

Another limitation of this study, especially in the case of tetanus antitoxin, is the fact that titrations of this antibody were not carried beyond a certain top antibody level. This made interpretation of results more difficult, as in most instances tetanus antitoxin levels higher than the maximum level tested for were obtained after basic prophylactic inoculation. It is quite possible that a difference in tetanus antitoxin levels would have been found between the two age groups had tetanus antitoxin determinations been carried to the highest level.

Other facts to be taken into consideration are the following: Different lots of the triple combined antigen were used in carrying out the basic inoculations. The antigenic capacity of different lots of the vaccine presumably differed somewhat, but not enough to affect the results significantly. The number of patients tested for antibody levels in both Series X and Series B decreased as time went on. However statistical analysis took due account of any error which may have been introduced by variation in the size of the groups tested.

The foregoing limitations do not invalidate previously drawn conclusions, but rather suggest possibilities for further investigation.

3. *Evaluation of Results of Prophylactic Inoculation Against Tetanus, Diphtheria and Pertussis in Newborn Infants:* The results of prophylactic inoculation against tetanus in newborn infants were highly satisfactory. It has been stressed by Miller[5] that "in pediatrics tetanus immunization should imply complete protection—the continued presence of antitoxin in concentration as high as can be attained transiently by prophylactic antitoxin." These conditions were met in this series of cases. Throughout the period of observation all patients had more than 0.1 units/cc. of tetanus antitoxin. The antibody titers achieved after inoculation were unusually high and were equalled only by other series of patients in which the same immunizing material was used.[4–6] It is clear that the tetanus toxoid contained in this preparation has great antigenic potency.

Diphtheria antitoxin titers attained by newborns after basic inoculations were not as high as those achieved in "older" children by the use of the same immunizing agent and following the same routine. However, the antibody levels observed in the younger age group after booster dose are to be considered as eminently satisfactory. The results of immunization against diphtheria have usually been gauged by the number of Schick-negative patients observed after inoculation. All of our newborn cases had antitoxin levels of 0.03 units/cc. or more after re-injection. This antitoxin level is 7½ times greater than the titer generally conceded as sufficient to induce Schick-negativity in the majority of individuals.[7]

The results of prophylactic inoculation of newborn infants against pertussis were not as good as those achieved by the "older" children with the use of the same vaccine. The number of young infants with pertussis agglutinin titers of 1:400 or more was never greater than 63%, even after administration of a booster dose. The proportion of newborn infants with "protective" titers was therefore far less than the 90% which apparently is the maximum obtainable with any dose and at any age.[5]

The relatively low percentage of children injected in the newborn period who showed agglutinin titers of 1:400 or more would lead to the assumption that many of them did not develop satisfactory immunity to pertussis after inoculation. However, it is known that a substantial number of patients with low pertussis agglutinin titers are found not to be susceptible when exposed to infection. Final judgment as to the results of prophylactic inoculation must be deferred until the degree of protection upon intimate familial exposure to whooping cough can be ascertained.

The question as to whether better results might be realized, if the amount of pertussis vaccine in the triple combined antigen were increased and the antigenic stimulus thus rendered more potent, cannot be answered without further investigation.

4. *Advisability of Routine Inoculations of Newborn Infants Against Tetanus, Diphtheria and Pertussis:* In conclusion, satisfactory immunization against diphtheria and tetanus and a significant degree of protection against pertussis may be realized by starting prophylactic inoculations in the newborn period. However, until more work is done and until the degree of clinical protection (after exposure to infection) afforded the individual can be evaluated, a conservative approach to the problem is urged.

If combined prophylactic inoculations are undertaken at the age of three months, immunity against diphtheria, tetanus and pertussis, in most cases, will be achieved by the age of five months, several months earlier than by following the conventional schedule in which injections are started at six to nine months of age.[8] The literature suggests that by the age of three months the critical period of immune mechanism

immaturity will presumably have been passed. Also, by the age of three months the levels of passively transmitted diphtheria antitoxin will have decreased sufficiently so as not to prevent the "sensitization" of the immune mechanisms following diphtheria toxoid injection.

The following schedule for prophylactic inoculation is recommended when "Alhydrox" is used:

*1st injection:* 0.5 cc. at the age of three months
*2nd injection:* 1.0 cc. at the age of four months
*3rd injection:* 1.0 cc. at the age of five months
*Booster dose:* 0.5 cc. at the age of 18 months

A booster dose of pertussis vaccine alone should be administered whenever an immunized child is exposed to whooping cough. Under these circumstances, a dose of not less than 20 billion H. pertussis organisms in saline should be injected.

## Summary

A comparison was made of antibody production by newborn infants and by older children following prophylactic inoculation against diphtheria, tetanus and pertussis. In all instances the same triple combined antigen ("Alhydrox") was used, and the same routine was followed. First injection of vaccine was administered to all newborn infants at seven days of age. Most of the "older" children were between six and 12 months of age at first injection.

Incidence and severity of systemic reactions to administration of the triple combined antigen increased with subsequent injections in newborn infants; the reverse was true of the "older" children. No such difference was found between the two age groups in local reactions to inoculation. Five sterile abscesses were observed in the newborns; none in the "older" children.

Pertussis agglutinin titers achieved after immunization were consistently higher (even after booster dose) in "older" children than in infants injected in the newborn period.

"Older" children produced significantly higher diphtheria antitoxin titers after prophylactic injection than the newborn infants. After administration of a booster dose, however, diphtheria antibody production in the two age groups was comparable.

No difference was found at any time in tetanus antitoxin levels achieved after inoculation by the newborn infants and the "older" children.

It was concluded that during the first year of life the capacity to produce antibodies in response to an antigenic stimulus increases with advancing age. It was felt, however, that in some instances the immunologic handicap due to tissue immaturity can be overcome if a sufficiently great antigenic stimulus is given.

Evaluation of antibody titers achieved by newborn infants after prophylactic injection of triple combined antigen reveals that the results of immunization against tetanus and diphtheria were satisfactory. The results of inoculation against pertussis were considered to be unsatisfactory, mainly because the proportion of infants who produced "protective" agglutinin titers fell far short of the 90% which is the maximum that can be expected.

A conservative approach to the problem of active immunization in early infancy is urged. It is suggested that until further work is done, routine prophylactic inoculations not be started before the age of three months.

ACKNOWLEDGEMENTS

We wish to acknowledge our indebtedness to Dr. Walter E. Ward, Medical Director of Cutter Laboratories, whose cooperation and assistance made this investigation possible. Our sincere appreciation is also extended to Mr. R. B. Clark, former Director, and to Dr. E. H. Newkom, present Director of Clinical Research, for their helpfulness and continued support.

REFERENCES

1. di Sant'Agnese, P. A., Combined immunization against diphtheria, tetanus and pertussis in newborn infants; production of antibodies in early infancy, PEDIATRICS 3:20, 1949.
2. Sako, W., Studies on pertussis immunization, J. Pediat. 30:29, 1947.
3. di Sant'Agnese, P. A., Combined immunization against diphtheria, tetanus and pertussis in newborn infants; duration of antibody levels; antibody titers after booster dose; effects of passive immunity to diphtheria on active immunization with diphtheria toxoid, PEDIATRICS 3:181, 1949.
4. di Sant'Agnese, P. A., Combined immunization against diphtheria, tetanus and pertussis in children over three months of age; including an evaluation of effectiveness of two immunizing agents, J. Pediat. 31:251, 1947.
5. Miller, J. J., Jr., Humber, J. B., and Dowrie, J. O., Immunization with combined diphtheria and tetanus toxoids (aluminum hydroxide-adsorbed) containing H. pertussis vaccine, J. Pediat. 24:281, 1944.
6. Miller, J. J., Jr., and Ryan, Mary Louise, Immunization with combined diphtheria and tetanus toxoids (aluminum hydroxide-adsorbed) containing H. pertussis vaccine; duration of serologic immunity, PEDIATRICS 1:8, 1948.
7. Ratner, B., Allergy, Anaphylaxis and Immunotherapy, Williams and Wilkins, Baltimore, 1943, p. 168.
8. Toomey, J. A., Report of Committee on Therapeutic Procedures for Acute Infectious Diseases and on Biologicals of the American Academy of Pediatrics, Evanston, Ill., 1947, p. 2.

SPANISH ABSTRACT

## Inmunizacion Combinada Contra Difteria, Tetanos y Pertusis en Infantes Recien Nacidos. III. Reiacion de Edad a la Produccion de Anticuerpo

Se hizo una comparación de producción de anticuerpo en infantes recién nacidos y en niños mayores después de la inoculación profiláctica contra difteria, tétanos y pertusis. En todos los casos el mismo antígeno combinado triplo, "Alhydrox" fué usado, y se siguió la misma rutina. La primera inyección de vacuna fué administrada a los infantes recién nacidos a los siete días de edad. La mayor parte de los niños "mayores" tenían de seis a 12 meses de edad cuando se les puso la primera inyección.

La incidencia y severidad de reacciones orgánicas a la administración del antígeno combinado triplo aumentó con inyecciones subsecuentes en infantes recién nacidos; lo contrario sucedió con niños "mayores." No se encontró tal diferencia entre los dos grupos de edad en reacciones locales a la inoculación. Cinco abscesos estériles fueron observados en los recién nacidos; ninguna en niños "mayores."

Los títulos de aglutinina de pertusis llevados a cabo después de la inmunización fueron consistentemente más altos (aún después de la dosis impulsadora) en niños "mayores" que en infantes inyectados recién nacidos. Los niños "mayores" produjeron títulos de antitoxina de difteria mucho más altos después de la inyección profiláctica que los infantes recién nacidos. Después de administrarles la dosis impulsardora, sin embargo, la producción de anticuerpo de difteria en los grupos de las dos edades fué comparable.

No se encontró ninguna diferencia en ningún tiempo en las cantidades de antitoxina de tétanos alcanzada después de la inoculación en los infantes recién nacidos y en niños "mayores."

Se llegó a la conclusión de que durante el primer año de vida la capacidad para producir anticuerpos en respuesta a un estímulo antigénico aumenta con el avance de edad. Se creyó, sin embargo,

que en algunos casos el impedimiento inmunológico debido a la falta de desarrollo del tejido se puede subsanar si se da un estímulo antigéno suficientemente grande.

La avaluación de los títulos de anticuerpo llevada a cabo en infantes recién nacidos después de la inyección profiláctica de antígeno combinada triplo revela que el resultado de inmunización contra tétanos y difteria fueron satisfactorios. Los resultados de inoculación contra la pertusis no se consideraron satisfactorios, principalmente a causa de que la proporción de infantes que produjeron títulos de aglutinina "protectiva" fué menos del 90% que es el máximo que se puede esperar.

Se incita un acercamiento conservativo al problema de inmunización activa en la temprana infancia. Se sugiere que hasta que se haga más trabajo, las inoculaciones profilácticas de rutina no deben de principiar antes de la edad de tres meses.

*3975 Broadway*

# PURE GRANULOMATOUS NOCARDIOSIS

## A New Form of Disseminated Infectious Granulomatosis with Massive Retroperitoneal Lymphadenopathy due to Nocardia Intracellularis (n. sp.)

*By* MARVIN L. WEIL, M.D., JOHN T. CUTTINO, M.D., AND ANNE M. MCCABE, A.B.
*Silver Springs, Md.*

IN 1913 Ewing[1] reported a series of cases simulating neoplasia in which he stressed the remarkable capacity of reticuloendothelial cells for proliferation in response to irritation. Later Oberling[2] reviewed six cases and established the general group of xanthogranulomata which consist of inflammatory tissue, infiltrated more or less extensively by foam cells containing cholesterol esters, cholesterol, and neutral fats. The abundant proliferation of histiocytic and fibrocytic elements in some areas suggested true tumor processes, but the xanthogranulomata are to be distinguished from xanthomata by their histologic polymorphism, which, on the whole, is that of an inflammation and not a tumor. Oberling regarded local inflammation and deranged cholesterol metabolism as the two main factors active in pathogenesis. One of the most characteristic sites of localization for this disturbance is the retroperitoneal space where tumor masses of considerable size may occur. Foot[3] reported an unusual giant cell lymphogranuloma from which was isolated an organism regarded as an actinomycete.

Retroperitoneal masses in children present problems of differential diagnosis which are of extreme difficulty to the clinician. The majority of these are neoplasms such as the lymphosarcomas or sympathicoblastomas, and an occasional case is classified with the reticuloendothelioses. Some, however, which clinically simulate malignant disease are ultimately found to be granulomatous in nature, the etiologic agent of which may be determined. The chief purpose of this report is to present the clinical details of a case which simulated neoplasia but which was proved to be a granuloma caused by a specific infectious agent.

### CASE REPORT

N. M. F., a 34-month-old, white female, was admitted to Duke Hospital with the chief complaint of an abdominal mass of two months' duration. The mother, father, and one 4-year-old brother were in good health. No history of tuberculosis or hereditary disease could be obtained. The patient had always been a "puny" child according to the parents, although photographs taken one year prior to the present illness show a healthy appearing youngster. At 8 months of age she had "dysentery," followed one month later by measles. During this period of her life she had eaten whatever food was proffered her, but only in small amounts. There was no other history of an acute infectious disease, operation or injury. The review of systems was entirely normal until the present illness. There was no history of night sweats, cough, chest pain, hemoptysis, or dyspnea.

She was breast fed until about 15 months of age and in so far as is known had only pasteurized

---

From the Departments of Pediatrics and Pathology Duke University School of Medicine and Duke Hospital, Durham, N.C.

Preliminary reports of this case were presented before the American Federation for Clinical Research, Southern Section[4] and the American Association of Pathologists and Bacteriologists.[5] Pathologic-anatomic, bacteriologic and infectivity studies have been reported in detail elsewhere.[6]

(Received for publication July 6, 1948.)

milk at home. She occasionally drank raw milk from herds which had been certified as free of tuberculosis by the local health authorities and she was also in contact with dogs, cows, horses, pigs, and chickens. All of these animals were in apparent good health at the time of the patient's present illness.

About two months prior to admission the child became anorexic, irritable and listless. She began vomiting after her meals and cried as though in pain when the abdomen was touched. One and one-

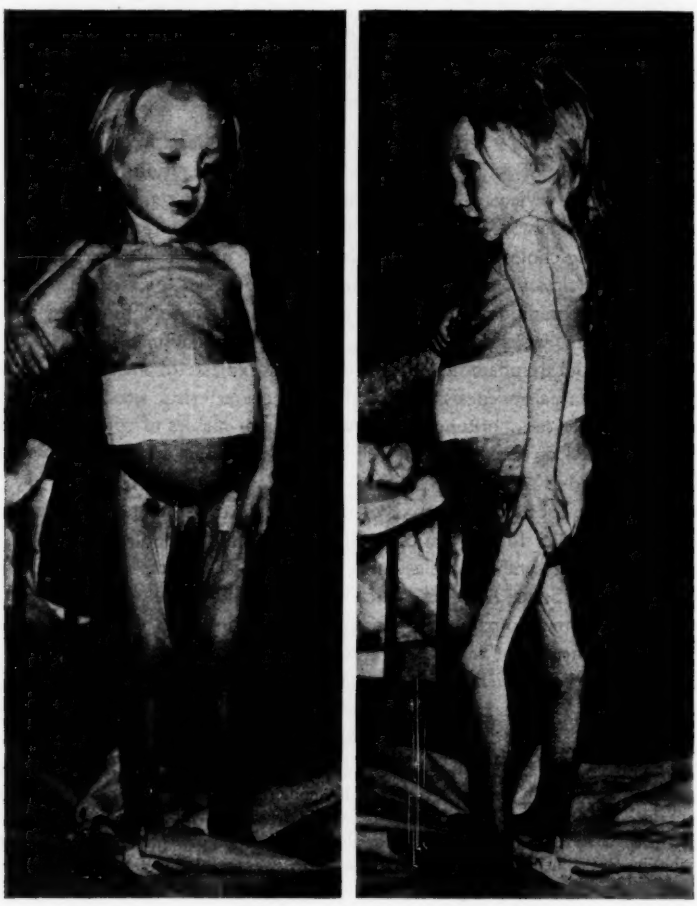

FIG. 1. Patient as she appeared three months after the onset of symptoms.

half months prior to admission an abdominal mass was noted and 1 month before admission, she was seen by her physician who reported the following: Weight 10 kg; urine, normal. Blood studies revealed: Hgb. 8.4 gm., RBC 3.1 million, WBC 20.15 thousand with 33% polynuclears, 62% lymphocytes, 3% eosinophils, 2% monocytes. A large mass was palpated in the abdomen. Roentgenogram of the chest was normal. She was given 225 ml. of whole blood without reaction. One month prior to admission gastrointestinal fluoroscopic studies with a barium meal had revealed no abnormality. Three weeks later intravenous urograms revealed a displaced left ureter but nothing

abnormal in excretory function. Because the child was thought to have a retroperitoneal sarcoma, deep roentgen therapy was given. On April 22d, the child weighed 8.7 kg., which indicated a known weight loss of 1.3 kg. in 34 days. For the three weeks prior to admission she passed only watery stools without blood and vomited following the ingestion of even small amounts of food. She was transferred to Duke Hospital for further study and treatment.

Physical examination on admission revealed a severely emaciated white girl (Figure 1) of 34 months with T. 38.1°C., P. 120, B.P., 86/46 mm. Hg. The skin was warm, loose, and dry; having almost no subcutaneous fat. Prominent veins were noted over the abdominal wall. No cyanosis, edema, or jaundice was present. A few shotty lymph nodes were felt in the left side of the neck, the left axilla, and both groins. The eyes, ears, nose and throat were normal; the teeth were carious. The heart and lungs were normal. The abdomen was protuberant. A firm, nodular, tender mass almost entirely filled the abdominal cavity, being palpable in both flanks and upper quadrants. The liver,

FIG. 2. Microscopic section of the lymph-node obtained by biopsy. Note great number of acid-fast organisms within the cytoplasm of characteristically reacting reticuloendothelial cells. Ziehl-Neelsen stain, X137.

spleen and kidneys could not be palpated. Genitalia were normal for her age. The joints were freely movable and no abnormalities of the skeletal structure or function were noted. The neurologic examination was normal except for a generalized weakness due to the emaciation. On admission Hgb. was 8.1 gm., RBC 4.2 million, WBC 19.36 thousand with 26% polynuclear neutrophils, 38% stabs, 19% juvenile neutrophils, 4.5% lymphocytes, 12.5% monocytes. Sternal marrow puncture revealed the bone marrow to be of normal cellularity and morphology.

Old tuberculin through a dilution of 1:10 was negative on intradermal injection. Other findings included: Schick test, 2 plus; Wassermann, Kline, Kahn and Mazzini reactions, negative; cholesterol 100 and 110 mg./100 cc. blood. NPN 26 mg./100 cc. blood; calcium 8.8 mg.; phosphorus, 4.1 mg.; $CO_2$ combining power, 56 vol. %; blood sugar, 93 mg.%; Weltmann coagulation band 3, total proteins 6.0 gm./100 cc. blood.

X-ray films of the chest revealed no abnormality. X-ray films of the skull showed it to be rather small for the patient's age and revealed considerable thinning of the skull bones. The pelvis and hip joints showed questionable loss of calcium. The long bones failed to show any abnormality or evidence of xanthomatosis.

The entire course in the hospital was afebrile except for rare elevations to 38.5° and 38.8°C. On the 3rd day a biopsy of the right inguinal nodes was performed. The specimen was interpreted as a

reticuloendotheliosis and on the 9th day an exploratory laparotomy was undertaken. Upon entering the abdominal cavity a moderate amount of odorless, turbid, yellowish fluid was found. The spleen, kidneys, and both lobes of the liver were found to be of normal size and consistency. The masses which had been palpated through the abdominal wall were found to be entirely retroperitoneal and extended throughout the whole posterior surface of the peritoneum. The mass was very firm and

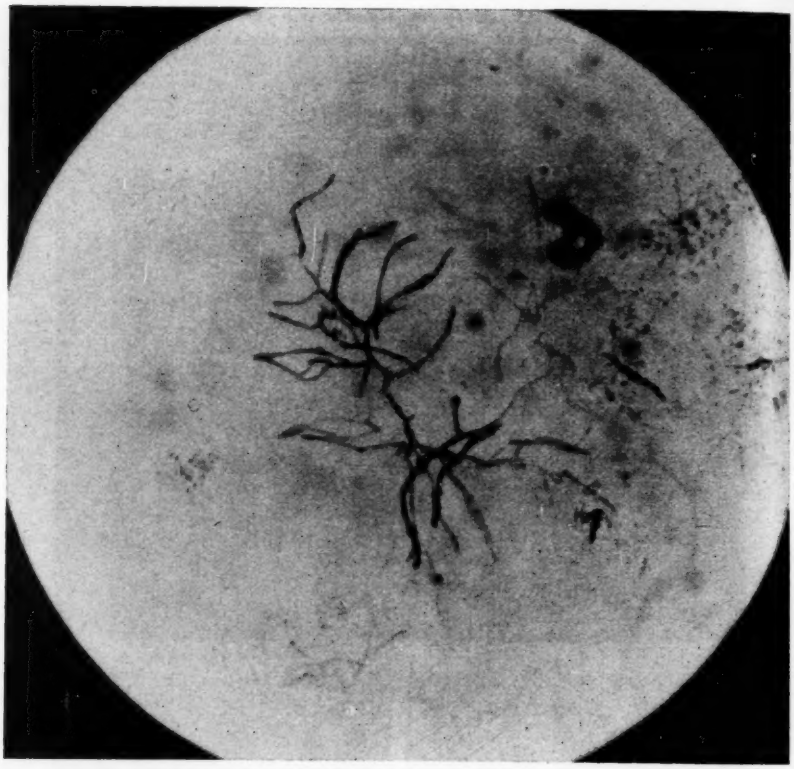

FIG. 3. Nocardia Intracellularis (n. sp.) from litmus milk after 30 days. Branching nature of organism is readily discernible Kinyoun Stain, X 1368.

nodular. No primary originating site could be determined. Biopsy of the retroperitoneal mass was performed.

Hemotoxylin and eosin stains of the biopsied material showed broad sheets and groups of large pale cells whose cytoplasm appeared granular, taking the hemotoxylin in a stippled manner. Focal groups of lymphoid tissue were interspersed between the pale staining cells. Fat stains contributed little to the general knowledge and the various lipodystrophies and xanthomatoses were considered in the differential diagnosis although no clinical evidence of such was found.

Bacterial stains first demonstrated the nature of the illness when the cytoplasm of the cells was found to contain many gram-positive acid fast rods. Lymph nodes from the left inguinal region were removed for biopsy and a portion used for culture and animal inoculation. Acid-fast smears of a $10^{-6}$ dilution of the macerated node revealed many organisms. Microscopic sections of a portion of the node used for biologic studies revealed changes similar to those already seen. There was a pure granulomatous lesion consisting only of proliferated macrophages which were replacing the entire

medullary portion of the node. Many macrophages were also found in the node capsule. The cytoplasm of these cells was loaded with pleomorphic acid-fast organisms. (Figure 2) There was no necrosis.

Stools, varying from 3 to 10 per day, were black (patient receiving iron), watery, with a few formed elements and no offensive odor. Microscopic studies revealed no ova, parasites, blood, pus or mucus; benzidine trace. Gmelin negative, Sudan positive, stool fat 30.49% of the dry weight. Acid-fast stains of the stool revealed many acid fast organisms singly and in clumps per high powered field. Small amounts of mucus which contained the organisms in even greater profusion began appearing with each stool. At this time the organisms were first isolated from the stool along with Monilia albicans.

Barium fluoroscopic studies revealed no significant abnormality of the esophagus, stomach, duodenum, or small bowel. The mucosal pattern was within normal limits for the age group and transit time was normal. Proctoscopic examination revealed normal mucosa except for several areas, 3 to 5 mm. in diameter, where the mucosa was granular, thickened and covered with a greyish fibrinous exudate. Two of these areas were 8 to 9 cm. from the anal sphincter. Biopsy revealed a nodular granulomatous lesion in the mucosa consisting of the typical large mononuculear phagocytes which caused some displacement of the adjacent intestinal glands. Occasional isolated cells of a similar nature which seemed to have no relation to the previously described nodule were also seen. There were numerous acid-fast organisms elsewhere in the mucosa and on its surface, apparently free in the tissue spaces and unrelated to phagocytes. The typical organisms were isolated on culture.

No acid-fast organisms could be demonstrated on smears of the nasal septum. Intradermal skin tests with 0.1 ml. avian tuberculin (Jensen-Salsbery Laboratories) gave no reaction. Appetite was consistently poor, but the child frequently called for mashed potatoes, bananas, and chocolate milk. There were several instances of coprophagia during the latter part of the illness.

Promin, 0.30 gm., was given orally each day beginning on May 23 with the hope of combating the acid-fast infection. Hgb. which was 13.6 gm. at this time rapidly fell to 11.5 cm. on May 25 and the promin was accordingly reduced to 0.20 gm./day given in divided doses. Under this regimen, Hgb. decreased very slowly and was supplemented from time to time with citrated whole blood transfusions. This dosage was discontinued on June 18 because of anemia and resumed on June 30. On May 29, 20,000 units of penicillin every 3 hours was begun and this was raised to 50,000 units every 3 hours on June 21. Neither of these drugs had beneficial effect. It was occasionally necessary to give codeine for relief of pain. Blood transfusions were also used. During the period of May 8th-13th five X-ray treatments of 50 R. units each were given over the abdominal mass without benefit. These were discontinued after the infectious origin of the case was established.

On May 21 the patient's serum failed to agglutinate organisms isolated from the lymph nodes. Later, serum gave agglutination through a dilution of 1:640. Serum drawn from a guinea pig and chicken six weeks after inoculation agglutinated the organisms in dilutions of 1:640 and 1:1280 respectively.

The admission weight of 8.7 kg. changed little, being 8.65 kg. on the day of death. The patient became weaker as her illness progressed, being unable to stand up and later unable to sit up. On July 8 respirations became shallow and gasping and then ceased entirely on the 78th hospital day. Postmortem cardiac puncture revealed 8 ml. straw colored pericardial fluid. Serum protein studies from cardiac blood by Dr. M. L. Dillon revealed: total proteins 5.08 gm./100 cc., with albumin 32.5%; alpha$_1$ 11.5%, alpha$_2$ 16.9%, beta 13.4%, gamma 25.7%. This is essentially a relative and absolute increase in alpha$_1$, alpha$_2$ and gamma globulin, and a decrease in albumin.

## Anatomic Findings

Autopsy: Body was emaciated. Abdomen was greatly distended. Only other external finding of note was the presence of enlarged axillary nodes. When the abdomen was opened a large quantity of chylous fluid escaped. There was a large mass in the retroperitoneal region which served to displace the abdominal viscera laterally and cephalad. Chylous material also was found in the pleural cavities.

The retroperitoneal mass measured 12 to 14 cm. in its greatest dimension. It consisted of a mass of enlarged and matted lymph nodes which had not lost their identity. The mass was soft and on section exhibited a yellow tissue in which large masses of caseation necrosis were seen. No char-

acteristic morphologic features could be made out grossly. The kidneys, pancreas, and adrenals were incorporated into the mass but not infiltrated. The lymph nodes of the mediastinal and left subclavian groups were enlarged and on section showed the same features with the exception that no necrosis was recognized. The spleen was slightly enlarged. The splenic pulp was dark red and the Malpighian bodies were markedly prominent. The small intestines were remarkable only in that the engorgement of the serosal lacteals was striking. However, throughout the course of the colon were numerous irregular ulcers with indurated edges. The floor of the ulcers presented a dirty greyish yellow color when the greenish mucoid covering was removed. The lymphoid follicles of the colon were prominent and the marginal lymph nodes were swollen. On section they also appeared yellow and homogeneous but no necrosis was noted.

The lungs were edematous but showed no additional gross lesions. The heart was grossly normal except for endocardial calcification at the base of the mitral valve. The liver was slightly enlarged and scattered throughout the parenchyma were tiny pale areas, otherwise no lesions were found. The gall bladder and biliary system showed nothing unusual. The pancreas showed appropriate size, shape and consistency. The kidneys showed no abnormality except for a mild dilatation of the pelves. The bladder was slightly distended by clear straw colored urine. Its mucosa was smooth and pale. The uterus, Fallopian tubes and ovaries showed an expected infantile state and no abnormality was noted. The brain weighted 890 gm. No abnormality of the brain or meninges was noted. The bone marrow was pale with small irregularly shaped lesions of homogeneous character.

Microscopic examination: The lymph nodes of the mesenteric and retroperitoneal group showed complete replacement of their architecture by sheets of irregularly shaped macrophages. The nuclei of these cells were usually pale and vesicular. However, many cells contained small hyperchromatic nuclei. The cytoplasm presented a bluish pink color. Many giant cells were found, most of which were of the Langhans type with peripherally placed nuclei. In the center of some giant cells were pale rounded structures which stained pink by eosin and in these areas the bluish appearance generally observed in the cytoplasm was not seen. In sections stained by Ziehl-Neelson technic, these macrophages were found to contain massive numbers of acid-fast bacilloid organisms. The large areas of necrosis found grossly were irregularly placed and did not conform to any specific location. A large artery carrying a recanalized thrombus was found.

Sections of the spleen showed a replacement of architecture by macrophages to a degree equal to that encountered in the lymph nodes. The macrophages were cytologically similar to those of the lymph node but, in the spleen about the central artery of the follicle, they assumed a concentric arrangement of such size as to suggest that these were the lesions mistaken for enlarged Malpighian bodies. Necrosis was not found in the spleen. In Ziehl-Neelson preparations one could again observe the massive numbers of acid-fast organisms within the macrophages.

Sections of the liver showed no parenchymatous lesion but scattered throughout were small lesions composed of concentrically arranged macrophages. The Kupfer cells were frequently swollen in appearance. With Ziehl-Neelson preparations the macrophages of the tuberculoid lesions as well as the Kupfer cells were found to contain massive numbers of acid-fast organisms.

Microscopic sections of the lungs confirmed the mild edema noted grossly and in addition, when Ziehl-Neelsen preparations were studied, the reticuloendothelial cells of the bronchial submuscosal lymphoid structures found in the vicinity of some of the larger arteries contained numerous acid fast organisms. It is to be emphasized that such lesions were not appreciable in routine hemotoxylin-eosin preparations.

Histologic sections of the colon taken from one of the ulcers showed a marked proliferation of macrophages in the lymphoid structures. In the margins and floor of the ulcer there was fibrosis with many nests of macrophages. These macrophages were cytologically similar to those of lymph nodes and the spleen in that they showed a bluish-pink cytoplasm with either large vesicular nuclei or small hyperchromatic nuclei. A few giant cells were seen. In addition a few scattered plasma cells and lymphocytes were recognized. No polymorphonuclear leukocytes were identified. About the ulcers there was a moderate fibroblastic healing reaction. Ziehl-Neelson stains showed that the macrophages contained massive numbers of acid fast organisms.

The lymphoid structure of the appendix also contained numerous reticuloendothelial cells in whose cytoplasm many acid fast organisms were found. The macrophages of the bone marrow contained many acid fast organisms.

Histologic study of other organs showed no lesions and a study of Ziehl-Neelson preparations failed to demonstrate acid fast organisms.

### Bacterial Studies

The organism isolated from the stools and a lymph node of the patient was aerobic, extremely acid fast, and gram-positive and grew in an easily fragmented branching form (Figure 3). Optimum growth was obtained at 37.5°C. The organism was killed in 10 min. at 60°C. Branching, similar to that of the aerobic acid fast Nocardia, could be demonstrated in Van Tiegham cell mounts as well as in broth and milk cultures. In smears from culture, the branching elements fragmented readily into cocco-bacillary and rod-like forms.

Glycerinated and fat-rich media were necessary for the favorable cultivation of the organism, although good growth was obtained with Sabouraud's media. On glycerinated egg medium and Bordet-Gengou agar, yellow, raised, smooth, and fairly confluent colonies appeared in 3 to 5 days. In beef extract broth plus 5% glycerin growth occurred in the form of a web-like clot at the bottom of the tube with extension of the growth part of the way up one side of the tube. The broth remained clear and there was no pellicle. Acid was produced in 5 to 10 days in glycerinated fermentation broths containing 1% of xylose or arabinose. No fermentation occurred with either lactose, dextrose, sucrose, mannite, trehalose, or sorbitol. Nitrates were reduced to nitrites, but indol production was negative.

After digestion for 30 minutes with N NaOH there was growth of the organism in 14 days.

On injection the organism produced a lesion in, but was not fatal for, guinea pigs, rats, and mice. It was not pathogenic for rabbits, frogs, goldfish and chickens.[6]

## Discussion

This case, which resembles a neoplastic process in many respects, illustrates how closely disease processes of infectious origin can resemble neoplasms. The clinical diagnosis would have been missed had it not been for the demonstration of acid fast organisms in the biopsy material and later in the stools. The discovery of acid fast organisms in such profusion in the stool might have afforded a clue to the disease process even in the absence of biopsy. It is noteworthy that several other reports of unusual acid fast organisms have been associated with remarkable clinico-pathologic pictures.[7,8]

The disease picture was that of a wasting disease associated with a large abdominal mass and was characterized by a granulomatous inflammatory response to an unusual acid fast organism, now regarded as a hitherto unrecognized form, Nocardia intracellularis, n.sp.[6] Study of the material has led us to feel justified in attributing the disease to the acid fast organism. The unusual lack of cellular reaction, other than reticuloendothelial proliferation and phagocytosis to the extensive proliferation of the organism, and its cultural characteristics, which resembled those of pathogenic and saprophytic bacteria as well as Nocardia, indicate that the organism is a member of a distinct group of rapidly growing, acid fast organisms of low pathogenicity. Further study will be required to establish the exact position of this group of organisms in the vague zone between Nocardia and Mycobacterium.

## Summary

A case of an infectious granulomatous disease, in which the clinical picture resembled that of a retroperitoneal tumor, is presented. The etiologic agent is shown to be an hitherto undescribed organism, Nocardia intracellularis, n.sp. The clinical similarity of this rare disease to xanthogranulomata and neoplasms is emphasized. The diagnosis rests primarily upon histopathologic studies of the lesions, especially with reference to intra-

cellular organisms. The condition may be suspected if atypical acid fast organisms are found in the stools of patients with clinically similar pictures.


REFERENCES

1. Ewing, Jr., Endothelioma of lymph nodes, J. M. Research **28**:1, 1913.
2. Oberling, C., Retroperitoneal xanthogranuloma, Am. J. Cancer **23**:477, 1935.
3. Foot, N. C., Report on case of unusual giant cell lymphogranuloma, Am. J. Clin. Path. **6**:278, 1936.
4. Weil, M. L., Cuttino, J. T., and McCabe, Anne M., Infection with unusual acid-fast organism, Proc. Am. Federation Clin. Research **3**:29, 1947.
5. Cuttino, J. T., McCabe, Anne M., and Weil, M. L., New form of granulomatous disease in man characterized by intracellular parasitism due to an as yet unidentified acid-fast organism, Am. J. Path. **23**:873, 1947.
6. Cuttino, J. T., and McCabe, Anne M., Pure granulomatous nocardiosis; new fungus disease distinguished by intracellular parasitism, Am. J. Path., in press.
7. Beaven, P. W., and Bayne-Jones, S., Mycobacterium, Ryan strain, isolated from pleural exudate, J. Infect. Dis. **49**:399, 1931.
8. Crail, H. W., Myelofibrosis, splenomegaly, and megakarocytic myelosis, Arch. Int. Med. **78**:14, 1946.



SPANISH ABSTRACT

## Nocardiosis Granulomatosa Pura

Se presenta un caso de una enfermedad granulomatosa infecciosa, en la cual el estado clínico se parecía al de un tumor retroperitoneal. Se muestra que el agente etiológico es hasta ahora un organismo que no se ha descrito, Nocardia intracellularis, n. sp. Se encuentra la similaridad clínica de esta rara enfermedad con el xantogranulomata y el neoplasma. La diagnosis descansa primariamente en los estudios histopatológicos de las lesiones, especialmente con referencia a los organismos intracellulares. La condición puede ser sospechada si se encuentran organismos resistentes al ácido atípico en las deposiciones de pacientes con condiciones clinicamente similares.


*8801 Colesville Rd.*

Pediatrics

VOLUME 3 MARCH 1949 NUMBER 3

## SPECIAL FEATURE SECTIONS

# THE PEDIATRICIAN AND THE PUBLIC

## AN OPEN FORUM

EDWARDS A. PARK, M.D., *Editor,* PAUL HARPER, *M.D., Associate*

*Statements appearing in this column do not necessarily reflect the opinion of the editors nor are they to be interpreted as the official opinion of the Academy.*

### INTRODUCTION

THE problem of health services for children of school age is particularly timely in view of current interest in such services. The editors of this column have asked several authorities in this field to state their opinion of the objectives of a school health service and to describe practical methods of attaining these goals. The first two letters in the current issue deal with this subject; other letters on health services for children of school age will be published in subsequent issues. Dr. James L. Wilson is professor of pediatrics at the University of Michigan; Dr. Jessie M. Bierman is professor of maternal and child health at the University of California School of Public Health; and Dr. Dorothy B. Nyswander is professor of Public Health Education in the same school, and the author of "Solving School Health Problems, the Astoria Demonstration Study," the Commonwealth Fund, 1942.

The last two letters are from Dr. Albert D. Kaiser, health officer of Rochester, New York. Dr. Kaiser has described the program of the Council of Rochester Regional Hospitals for improving medical care in the 11 counties served by the member hospitals in the June issue of this column. His first letter in this issue describes how these services might be extended if additional funds were available. His second communication serves to make clear what was meant by "institutes conducted for . . . governing boards" as described in the eighth paragraph of his first letter.

January 18, 1949

DEAR DR. PARK:

I am concerned that a trend that seems superficially commendable in our school health program toward more complete study of the individual child's health problems may lead to wasteful effort which might be better expended in other directions.

School health activities in this country have without doubt contributed immensely to

public welfare and in recent years a great deal more attention is being given to extending such activities much further. The aggregations of children in our school system offer obvious and great opportunities for public health activities. In general, school health activities deal with: (1) the prevention of cross infection, made greater by the school system itself, and the control of other health hazards inherent in the school system; (2) education of the child and parents in health problems; (3) the actual care of the health of the individual child. There is a constant desire by many well-meaning people, particularly medical laymen, to expand and improve particularly the programs for the care of the health of the individual child to such an extent that it seems to me necessary for physicians with intimate experience in the technic of diagnosis and treatment to define more clearly the practical limits of such activities.

There is no question at all as to the need of public health activities to prevent the hazards inherent in the aggregations of children in the schools, and the opportunities for education of parent and child in health problems are obvious. There should be more question, however, as to how far the actual care of the individual child's health should be carried out within the school system and better definition of its practical scope should be made. It seems to me that if attempts are made to set up in the school health systems more than good screening processes for the detection of a limited number of remediable conditions which can be revealed by such studies, that illogical and wasteful efforts will result. Thoroughness is not necessarily a virtue and meticulous care in examination of each child, though wise and necessary is out of place in the schoolhouse except where no other community health resources are available or, and this is important, can be devised.

As in many other public health activities such as "well baby conferences" and immunization clinics, there is an inevitable conflict of opinion between those who believe that only through the private practice of medicine can good health care be obtained, and those who are more impressed with the opportunities of "socialized medicine." Although I personally hope there will never come a time when a universal state-supported sytsem of medicine will be offered free to all, nevertheless I do not want to enter into the discussion of the relative merits of so-called socialized medicine and private practice. I wish to consider only the advantages and disadvantages of the diagnosis and treatment of health problems of the individual child within the school system.

We should start with a statement of the general principles that are the basis for the ideal care of the individual child. The ideal for quality, and therefore to a great extent for economy, would be the continuous preventive diagnostic and therapeutic medical care of each child's physical and mental health, with one continuous record from infancy throughout childhood, by one competent supervising physician. The care of the child in health and in disease should not be separated; the diagnosis and the treatment of illness should not be separated; the different technics of diagnosis, parent conferences, physical examination, and laboratory study, should not be separated.

There are rare circumstances where continuous care by one physician or group of physicians for many years can be carried out, since the movement of people in this country from one community to another is very great and inevitable conflicts of personalities bring about quite proper changes from one physician to another. However, for long-time planning towards improving the child health, these are reasonable principles which we should constantly attempt to approach.

Wherever health care is discontinuous and delegated to different physicians, each new

physician involved must reaccumulate certain data, must learn all over again independently the personality and habits of each individual patient and his parents. A health record system is not carried by an individual as his private property and no record system in any case is really a complete substitute for memory. We must point out to the public and interested people that the physician who has cared for the sick child can more wisely decide on the time and degree of immunization procedures and feeding programs, and that the physician who has immunized the child and regulated his feeding as an infant and has dealt with his minor upsets, is thereby better qualified to take care of him when he is sick.

Although the separation of the child in health and in disease is disadvantageous to the quality of care, the separation of the technics of diagnosis and of treatment is even more wasteful. When faults diagnosed by one physician in one place are sent for correction to a different physician in a different place, confusion and gross inefficiency arise. It must be emphasized to the laity that no good physician is going to undertake therapeutic measures on the basis of someone else's diagnostic technics unless he himself checks those diagnostic technics. Having it done twice each time thoroughly and skillfully is, therefore, obviously inefficient.

The separation of the different technics of diagnosis, that is, history-taking, physical examination, and laboratory study is likewise quite impractical and wasteful and leads to poor quality of care. Many lay people are altogether too much impressed by the value of physical examinations alone. We have perhaps over-taught them in past years in our efforts to get the laity to accept more than symptomatic treatment. Now it is necessary to re-educate many interested lay people as to the limitations of physical examination and point out that to detect disease in its incipiency, the technics of observation, percussion, auscultation, palpation, and measurement are usually quite inadequate. Our ability to discover by physical examination alone herniae, hemorrhoids, systolic heart murmurs, adenopathy, etc., is clear enough, and our ability to detect faults in vision and in hearing is also thoroughly established; but to any pediatrician it is obvious how important it is that such technics of examination be coordinated step by step by conferences with the parents. Medical "history taking" done properly is a time-consuming diagnostic technic, one which requires a great deal of skill, even more than in physical examination, and cannot be reduced to a simple yet dependable form, although certain routine data can be collected by a clerical assistant.

It is difficult but important to impress upon lay people who are more and more influencing the organization of medical care, the fact that laboratory technics by themselves, though of little value until coordinated with history-taking and physical examination, are nevertheless necessary as part of any examination. Confusion about this was strikingly evident during the war when enthusiastic nutritionists eagerly sought some blood or urine chemical analysis to define and diagnose malnutrition. It is even now difficult to convince people that a sample of blood and urine is not sufficient to bring us to a definition of one child's state of nutrition. However, laboratory and X-ray procedures coordinated with the other technics of diagnosis are of increasing importance. Whenever physical examination alone is relied upon for the detection of early ill health, failure is probable since it is obvious that only gross abnormalities can be so detected and that early discovery of disease is unlikely. When history-taking and physical examination are thoroughly and wisely combined but laboratory work omitted, inefficiencies again arise. Few school diagnostic facilities include laboratories and X-ray equipment.

There are intrinsic disadvantages in an incomplete health examination in the school which must be recognized and reduced as much as possible. One is the great danger of giving false security to parents. If physical examination is relied on alone or physical examination and history alone, a complete diagnostic study is not carried out; the parents may be satisfied that their children have been given medical examinations and feel relaxed about the matter. Either screening tests, the limitations of which are frankly explained to parents are best, or the ultimate in practical thoroughness should be sought.

Another disadvantage in incomplete examinations is the very serious one related to parents' natural anxiety and therefore possible over-solicitude when there is any discussion with them of possible ills before the physician himself has reached his own conclusions. Report of a suggestion of heart disease or possible curvature of the spine, or whatnot, given to the parents with a warning and advice that they investigate it, cannot fail to bring about great anxiety. Sometimes, of course, it is quite necessary that such a situation arises. Nevertheless, it is always wiser for a physician who detects only a suggestion of a difficulty to go ahead quietly and come to a conclusion on complete evidence before he discusses the whole situation with the parents. Physicians well know that many mothers, when told that there is possibility of heart disease in their child, will never quite forget it, no matter how many other doctors reassure them, and that this suspicion and worry will bring about deleterious changes in the attitude of such mothers towards their child-rearing problems.

Another handicap in a school health system is the fact that the most crucial time for preventive and therapeutic health activities is during our patient's infancy. Our school system completely misses the child during the time when his immunization procedures should have been completed and during the critical years when the greatest incidence of illness and malnutrition occurs. Even if a complete medical care program were developed within our school system, unless we can plan another one for the infant age, we face a great deviation from the ideal at which we must aim.

What end then is logical to be sought in the development of health activities for the individual child in the school system? We should not plan to make any system for the care of the individual child's health in the school system into more than a screening process, unless we propose to go all the way to complete medical care. In other words, a complete physical examination should be done, coordinated with a complete history, X-ray and laboratory work as necessary, followed by proper therapy, carried out at the same time by the same physician hired by the school system. Any great deviation from such a process brings about waste and confusion, poor care, and reduplication of effort even though it may be defended as better than nothing. Do we want to build up within our school system a complete medical care program? This would necessarily be something such as is called "socialized medicine." Regardless of our feeling towards such a plan in itself, is the school system the right place? What then should we do if we admit that it is not yet practical for every child, regardless of his parents' economic or intellectual status, to be given continuous care by a private physician in his own office?

This brings us to the whole question of improvement of the practice of medicine for the individual patient in this country and it is not appropriate to expand such a discussion in this letter. It is clear that isolated private practice, through economic and organizational difficulties, has as yet failed at a complete solution to the problem, although in group practice in many places an approach to a solution for certain economic groups can be seen since the efficiency of coordinated activities of different specialists and

immediately available laboratory and X-ray facilities is gained. More and more it is evident that there is a distinct trend to hospitalize cases of even minor illnesses. Small homes, lack of aunts and grandparents as nurses, cost and shortage of trained nurses, more complex as well as effective therapy, all contribute to this trend. The hospital plays a constantly more important role in community health. It seems advisable therefore to plan that any community health efforts that include the diagnosis and treatment of disease and the health care of the individual be carried out in close association with hospitals where facilities for complete examination and history-taking, X-ray studies, laboratory work with all the expensive equipment, is already available and where the final stage of caring for illness in its acute serious form can be performed. Since private group practice organizations could be planned in or near hospitals, this does not need to be only a tax-supported plan.

Regardless of the relatively excellent level of health in this country compared with others, there is no question that great improvement and more general use of the technics of diagnosis and treatment of disease in early stages must be sought, together with an urgent attempt to reduce the costs. It seems to me far wiser for plans to be made for such procedures to be carried out by physicians, whether private or community-supported, closely associated with hospitals rather than within the school system. I believe we as physicians should attempt to direct the efforts of the many sincere persons, eager to improve child health, away from too great concentration on the school system and towards an improvement of other more suitable community health resources.

However, all this argument by no means should imply that attention to the individual child's health in the school system is wrong. It is attempted only to indicate how clearly limited and intelligently superficial it should be. The school health examination of the individual child should be kept deliberately a screening process with attention directed only toward the relatively few physical and emotional faults that such procedures can detect. It should be realized and emphasized that any effort towards real thoroughness and completely satisfactory school health examination would be ill-advised and that it would be far wiser to direct our energies towards organizing individual health activities under some better circumstances.

Sincerely yours,

(signed) JAMES L. WILSON, M.D.

January 15, 1949

DEAR DR. HARPER:

As a result of the increasing concern of pediatricians in community child health, we hope that a better understanding and greater interest in the special health problems of the child in school will be forthcoming. This would seem to be highly desirable because, on the whole, school health has been the least effective of our community health programs for children.

Why is this the case? The familiar arguments of lack of public support (funds) and of administrative problems (school vs. health department administration) come to mind. They are admittedly important. But isn't there another equally important reason which is discomforting to us in the medical profession—especially to us pediatricians? Who is responsible for the low status of the *medical functions* in the schools? In this field there has been very little of the kind of inspired medical leadership which has contributed so much to the solution of other important health problems in our country.

There is evidence that public support for substantial increases in funds for school health may not be too far away. The rapid increase in joint planning between departments of health, of education, and of community health groups in all parts of the country give promise of an eventual solution to many of the vexing problems of administrative authority.

But where will administrators be able to obtain the guidance which is necessary to insure that the medical aspects of these expanding programs will be of such quality that they will really serve the needs of children?

The work of the committees on School Health and on Cooperation With Non-medical Groups indicates that the Academy of Pediatrics recognizes that pediatricians have responsibility in school health. But in spite of the sound recommendations of these committees, there are far too few pediatricians actively engaged in this field.

Some idea of the kind of medical leadership which is necessary can be obtained by a brief review of some of the newer concepts of the physician's role in the School Health Program.

The differences between the philosophy and practices which dominated the school health field up to recent years and those of the present may be readily seen to be juxtaposing a few items which deal with the *medical aspects* of the school health program. Needless to say, similar contrasts are evident in other phases, such as the changes that are being urged in the teaching of health in the classroom; the emphasis on mental health in preparation of teachers; the joint planning of the program between the schools, health departments and other community agencies, and education of children with physical handicaps.

CHANGING CONCEPTS IN THE PHYSICIAN'S ROLE IN THE SCHOOL HEALTH PROGRAM

| OLDER CONCEPTS | NEWER CONCEPTS |
|---|---|
| Status of the Physician in the School | Status of the Physician in the School |
| a. An "appendage" with no real connection with the primary work of the school. | a. A responsible member of the staff who participates in planning all parts of the school program affecting the physical, emotional, and social health of children and staff. |
| Primary Function of the Physician | Primary Function of the Physician |
| a. To assist in control of communicable diseases.<br>b. To identify children with physical defects. | a. To give medical guidance in the development of a school environment and an experience which will contribute to the healthy development of children, and to give specific help to children with health problems. |
| Procedures for selecting individual children for attention by the physician: | Procedures for selecting individual children for attention by the physician: |
| a. Routine examinations of all children in selected grades or<br>b. Annual examinations of all children without any selection. | a. Only children entering a new school for the first time who do not have a record showing a recent medical examination by a physician in private practice or in a clinic.<br>b. Children selected on the basis of a regularly programmed conference between nurse and teacher as presenting a health problem. |
| Technics of medical examination: | Technics of medical examination: |
| The technics used can hardly be signified by the term "medical examination." "Medical in- | Technics grow out of a philosophy that action in behalf of a child will be taken when it is |

spection" is more nearly applicable. There were (and still are in some localities) two methods used to "examine" the children.

a. The physician sees from 15 to 30 or more children per hour.
b. A "team" of physicians examine the child on a specialized basis.

The above procedures are characterized by 1) lack of history data; 2) absence of parents; 3) absence of teacher; 4) absence of written interpretations to the school personnel.

"Follow-up" Procedures

After the hurried inspections by the physician, the "follow-up" work was left almost entirely to the nurse. The nurse was guided in her approach to the parent by a "code" on the medical record which indicated the degree of severity of the health condition discovered.

based on understanding by all persons who must contribute to that action. The "examination" *per se* becomes a *conference* which is characterized by:

a. Sufficient time to obtain history and questions from parent who is present.
b. Attention to observational data reported by teacher who is present or who has recorded her observations.
c. An examination which will enable the physician to understand the nature of the child's problem.
d. Planning with teacher, nurse, and parent as to *how, when,* and *where* aid can be obtained for the child.
e. Written suggestions to nurse and teacher as to ways they can help the parents and child.

"Follow-up" Procedures

The physician assumes responsibility for indicating both orally and in writing on the cumulative health records, his recommendations to teacher and nurse.

The physician develops relationships with private physicians, out-patient clinics, the health department, and other community groups to establish 1. better understanding of the facilities that are needed for diagnosis and treatment; 2. the kinds of reports needed by the school to help in supervising the child's life in school and 3. a basis for exchange of information important to the child's health.

The physician confers with persons both within and without the school concerning a child's health problem when it appears that he, rather than the nurse or teacher, may be more effective.

The modern approach to school health presents a great opportunity for physicians who understand the emotional and social as well as the physical aspects of the health needs of children and a challenge to medical education to supply us with more such physicians. At the present time probably the leaders from the pediatric field could be counted as the fingers of one hand.

(signed) JESSIE M. BIERMAN, M.D.
(signed) DOROTHY B. NYSWANDER, Ph.D.

December 27, 1948

DEAR DR. PARK:

I appreciate your letter and the opportunity to tell you more about our educational program in the regional hospital experiment in the Rochester area.

Our program thus far has been directed to the existing hospitals in the 11 county areas. There are about 30 general hospitals varying in size from 30-bed capacity to over 200 beds. Practically all of the physicians residing in these small towns and in the adjacent

rural areas are connected with one or more of these hospitals. It seemed advisable, therefore, to contact them as hospital staff members rather than as independent practitioners.

In a few instances we found a small hospital, with a staff of 15 to 25 physicians, had already provided excellent facilities for rendering good medical care and also that some consideration had been given to the proper selection of qualified physicians to carry on effectively the various medical services needed in a small community. However, in the majority of the existing hospitals certain essential facilities were either lacking or inadequately administered. Usually qualified medical personnel was not available for all types of service.

To correct this situation, additional properly qualified medical personnel is necessary or else postgraduate educational opportunities should be offered the physicians now connected with these hospitals. In this capacity the medical school and allied hospitals can be of great assistance.

The methods employed thus far in our experiment consist of monthly clinical conferences in the area hospital in which a medical teacher from the medical center participates; postgraduate courses, usually short, for area physicians, on a variety of subjects; offering fellowships to properly selected physicians who seek to improve their training in a special field; rotation of internes and residents to hospitals large enough to warrant such a service. In addition, consultive services can be made available from the medical center in pathology and radiology.

To carry out a continuing program of this sort and reach from 10 to 25 small hospitals requires organization and financial support. If it were limited to pediatric or obstetric training it could be managed on a departmental basis, but where the broad fields of medical practice are covered it is necessary to have an organization with an executive staff to direct these services as they flow from the medical center to the area.

Specialized groups other than physicians also need services of this type if all of the hospital facilities are to be improved. Nurses, medical record librarians, nutrition workers and others benefit greatly if opportunities are provided for further training in these fields. Here, too, the medical center furnishes the teaching facilities.

It has been our experience that improved medical service is dependent upon intelligent and cooperative support from hospital administrators and governing boards. In some instances gross deficiencies in medical care practices were either not known to governing boards or else the appointed individuals were not concerned about medical practices in their hospital and in the community. Institutes conducted for hospital administrators and for governing boards have proved of great value to the participants and have improved the relationship between administrative and professional departments.

Hospital organization, finance, recording keeping, nursing, etc., are well nigh inseparable from the quality of medical care. The objectives of medical education cannot be fully realized without attention to the more material aspects of hospital organization and operation.

The grant from the Commonwealth Fund is inadequate to supply all of these needed services. If additional funds were available, the educational activities could be increased, to cover all of the hospital services, professional and administrative.

The medical school and several of the large general hospitals in Rochester have been most cooperative in this program. A restricted budget in every large institution prevents complete utilization of the teaching facilities in these institutions for the regional

hospitals. An ideal program would require additional funds to employ part-time teachers in the medical and allied fields if the educational program were made available to the small town hospitals and rural physicians.

The experiment has demonstrated the feasibility and almost immediate success of this educational program for an area of considerable size. Intensification of the methods described can bring about a greater improvement but it must be a continuous program rather than a sporadic one.

I believe it is a pattern that could be used in most of the states, with such modifications as are necessary, depending upon the medical facilities existing in a large center. Even in the absence of a medical school in large centers, the average city general hospital has, I am sure, in most instances, the personnel to assist the small hospitals to improve their hospital facilities and their educational opportunities.

It is my belief that some of the inadequacies in medical care known to exist in smaller communities could be met in a regional health program. Utilizing the hospital offers a more direct approach to the problem and promises to bring substantial benefits to communities where such a program is carried on.

Very sincerely yours,

(signed) ALBERT D. KAISER

January 6, 1949

DEAR DR. PARK:

I am glad to explain more fully what is meant by institutes in our regional program. We use this term for conferences of various groups to give instruction in hospital or medical problems that particularly concern the group involved. For example, the institutes conducted for hospital administrators cover a wide field of administrative problems such as hospital personnel, bookkeeping, accounting, purchasing, public relations, etc. Leading hospital administrators from nearby institutions, as well as nationally known leaders, are brought to Rochester to conduct these institutes.

Specifically, to enlarge on the paragraph that deals with institutes for governing boards, the following plan has been adopted. Governing board members of three or four area hospitals are brought together at a convenient meeting place for a half day's session. A group leader, usually a qualified hospital authority, is sent to the meeting. In a rather informal way hospital problems are discussed and particular stress is placed on the responsibilities a board member assumes when he accepts membership on a hospital board. At these institutes laymen become acquainted with the real difficulties that exist in hospitals. Not only are they instructed in the business aspects of hospital management but they are familiarized with the every day medical practices which in some small hospitals need revision. Thus far, these institutes or group meetings have been appreciated by laymen connected with hospital boards.

I hope this explanation can be fitted into the paragraph dealing with institutes for governing boards.

Kindest regards.

(signed) ALBERT D. KAISER

# TRENDS

## IN HEALTH LEGISLATION AND ADMINISTRATION

*By* JOHN P. HUBBARD, M.D., *Contributing Editor*

*This and subsequent descriptions of events and trends are intended to be unbiased and factual, presenting both sides of controvercial matters so that conclusions may be formed from critical appraisal of things as they are. These statements do not necessarily reflect the opinion of the writer nor are they to be interpreted as official opinion of the Academy.*

AS GENERALLY expected, the proponents of national compulsory health insurance lost no time after the opening of the 81st Congress.

In his State of the Union Address delivered to Congress on January 5, 1949, President Truman called again for legislation for a national health program—a request he made in his first health message to Congress November 19, 1945. At that time, three years ago, he said:

"In the past, the benefits of modern medical science have not been enjoyed by our citizens with any degree of equality. Nor are they today. Nor will they be in the future unless Government is bold enough to do something about it.

"People with low or moderate incomes do not get the same medical attention as those with high incomes. The poor have more sickness, but they get less medical care. People who live in rural areas do not get the same amount or quality of medical attention as those who live in our cities.

"Our new economic bill of rights should mean health security for all, regardless of residence, station, or race—everywhere in the United States."

On the same day (November 19, 1945) the Wagner-Murray-Dingell Bill was introduced as S. 1606. After extensive hearings and some modifications, a similar bill (S. 1320) was introduced in the 80th Congress by Senator Murray with the additional sponsorship of Senators Pepper, Chavez, Taylor and McGrath, all Democrats.

In his message to the Democratic 81st Congress President Truman said:

"We must spare no effort to raise the general level of health in this country. In a nation as rich as ours, it is a shocking fact that tens of millions lack adequate medical care. We are short of doctors, hospitals, and nurses. We must remedy these shortages. Moreover, we need—and we must have without further delay—a system of prepaid medical insurance which will enable every American to afford good medical care."

On the same day Senator Murray introduced for himself, and senators Wagner, Pepper, Chavez, Taylor and McGrath a bill S. 5, "to provide a national health insurance and public health program." Two identical bills had already been introduced in the House, HR. 345 by Representative Celler and HR. 783 by Representative Dingell. All three bills are exact copies of last year's bill, S. 1320. (Copies of these bills may be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D.C., or from the committees to which they have been referred.)

The Labor and Public Welfare Committee, to which all health legislation is referred in the Senate, now has an eight to five Democratic majority under the chairmanship of Senator Thomas (Utah), having previously had an eight to five Republican majority under the chairmanship of Senator Taft. Its Democratic membership shows a decidedly liberal complexion: Senators Thomas, Humphrey, Douglas, Pepper, Murray, Neely, Hill

and Withers; its Republican membership consist of Senators Taft, Aiken, Smith, Morse and Donnell.

On the House side it is of interest, and possibly of considerable significance, that S. 345 (Rep. Celler's bill) was referred to the House Ways and Means Committee which handled the same type of legislation in the 80th Congress, while at the same time HR. 783 (Rep. Dingell's bill) was referred to the Interstate and Foreign Commerce Committee. In the latter committee it may be anticipated that the measure will be reported favorably to the House floor faster and with fewer restrictive changes than might be true in the Ways and Means Committee.

In the deluge of bills introduced during the opening days of the 81st Congress, is also to be found the Local Public Health Unit Bill, introduced in the Senate by Senator Chapman (S. 132) and into the House by Representative Dollivar (HR. 785). This is the same measure which was introduced in the 80th Congress by Senator Saltanstall "to assist the states in the development and maintenance of local public health units." This bill received favorable consideration in the 80th Congress and can be expected to have favorable attention again.

It is noteworthy that among the record volume of approximately 1500 bills, including scores of measures in the field of public health, medical care and hospitalization, there did not appear the National Child Research Institute Bill or the School Health Services Bill, both of which were published in draft form a month ago in this column and both of which would greatly enhance the activities and position of the Children's Bureau. Also lacking in this list was any measure specifically for Federal aid to medical education.

As a clue to the possible further development of health legislation in the 81st Congress, we wish to quote from a report published weekly by Mr. Gerald G. Gross,* a keen observer in Washington:

"Florida's Senator Pepper, a co-sponsor of the Murray-Wagner-Dingell bill, gave a little interview Thursday which allowed a cat to pop out of the Administration's strategy bag. Pepper said he and Senators Murray and Humphrey (all three are members of Labor and Public Welfare Committee) are working on a scheme to broaden the already broad M-W-D bill. The idea is to have this measure provide not only for compulsory health insurance but for Federal aid to medical education (also nursing and dental), public health services expansion, construction of more hospitals and more subsidization of medical research as well. In other words, to make a bitter dish more palatable, Pepper and Murray and other backers of M-W-D being realistic enough to appreciate that it will be a formidable task, indeed, to maneuver a straight, unsweetened dose of health insurance through both houses of Congress.

"Implication of the Pepper interview was that the scheme was the Senators' and endorsement by Federal Security Administrator Ewing and President Truman awaited. What's probably closer to the truth is that Ewing cooked up the idea himself and tossed it into the Senator's receptive laps for them to nurture and receive credit therefor. In recent weeks Ewing has conferred with many medical, dental and nursing educators, hospital leaders, public health authorities and other spokesmen for non-governmental enterprise. Undoubtedly the idea was germinating more than two weeks ago, when Ewing said top priority should be given in this Congress to Federal assistance of professional education in the medical and allied sciences (WRMS No. 83). Note carefully that this and other features which Pepper, Murray, et al, would incorporate in an expanded M-W-D bill—greater funds for Hill-Burton hospital construction, local public health units, private medical research, etc.—are not only non-controversial but actually desired by the prospective beneficiaries who, in the majority are opponents of compulsory health insurance.

"OUTLOOK FOR THIS 'COMPROMISE' The omnibus plan if welded into bill form and

* Washington Report on the Medical Sciences, No. 85, January 17, 1949, published each Monday by Gerald G. Gross, Editor, Hibbs Building, Washington 5, D.C.

introduced, probably will accomplish little more than to demonstrate that proponents of M-W-D hold in wholesome respect the rising tide of opposition to that piece of legislation. It is doubtful whether any fortnight in any session of Congress has witnessed as many critical inserts in the Congressional Record appendix as appeared in the first two weeks of the present session. The various organizations pressing for government financial assistance of local health units, research, professional education, hospital expansion and so on may be 'warned' that their chances of success will be reduced—if not killed—unless they take M-W-D in the bargain. But it doesn't take a seer to predict what their answer will be."

As a further clue to the manner in which the debate will be conducted, it is of interest to note some of the organizations and agencies which have declared themselves for compulsory health insurance and which are openly opposed. The following have come out for compulsory health insurance: American Federation of Labor, American Veterans' Committee, Congress of Industrial Organizations, Committee for the Nation's Health, National Association for Advancement of Colored People, National Council of Catholic Women, National Council of Jewish Women, National Council of Negro Women, National Farmers Union, National Women's Trade Union League, Railroad Brotherhoods, Women's International League for Peace and Freedom.

The following have declared themselves against compulsory health insurance: American Medical Association, American Farm Bureau Federation, American Legion, Chamber of Commerce, Committee for Constitutional Government, Inc., National Grange, National Physicians' Committee.

JOSEPH S. WALL, M.D., *Chairman*
*Committee on Legislation*

# PUBLIC HEALTH, NURSING AND MEDICAL SOCIAL WORK

LEONA BAUMGARTNER, M.D., *Contributing Editor*

TO THE busy practitioner working with six to 12-year olds and their parents, the new booklet YOUR CHILD FROM SIX TO TWELVE, put out by the Federal Children's Bureau, will be a welcome aid. To those who have searched for materials about these children, it is evident that far too little has been written about them and particularly about their emotional and social growth and development at this period. Yet six to 12-year-old youngsters account for more than a third of all the nation's 45 million children.

While this new booklet of the Children's Bureau was prepared primarily for parents, YOUR CHILD FROM SIX TO TWELVE has much to commend it to physicians, nurses, and other professional people working with children. The book attempts successfully to appraise the six to 12-year old in his own home—exactly the subject with which physicians, nurses, and other professional people are so often confronted. And certainly few physicians have the time to answer the many questions that parents ask. Katharine F. Lenroot, Chief of the Children's Bureau, has summarized the purpose and scope of the book very well when she has said: "The booklet offers no magic formula to parents on the care of their children. But it does help us see why children between six and 12 behave the way they do. Why they want to do some things and not others. What their physical and mental limitations are. How their abilities can best be developed as they grow older. Above all, the booklet shows how children at this age need and respond to real understanding and respect."

This booklet, like others prepared by the Children's Bureau for parents, is written in a quite informal style and has many common sense suggestions about dealing with children of these ages. Some of the things discussed are: What six to 12-year olds are like, what successful parenthood involves, how families influence children's social adjustments, what play means in the life of a child, helping children make the most of their mental ability, when home and school get together, fear, worries and frustrations, pursuits and hobbies, developing wholesome sex attitudes, growth in middle childhood, keeping the child healthy, and the sick child.

The booklet was prepared by members of the Children's Bureau staff, under the direction of Dr. Katherine Bain, and a group of pediatricians, psychiatrists, educators, and other specialists, including an official representative of the American Academy of Pediatrics, reviewed it in manuscript further to insure that it presents the best practices in child care.

YOUR CHILD FROM SIX TO TWELVE completes a series of five booklets put out by the Children's Bureau for parents on child care, from the prenatal period through adolescence. The best known of these is INFANT CARE which has passed the 23 million mark in the number of copies distributed since the first of its various versions was published in 1914.

Single copies of YOUR CHILD FROM SIX TO TWELVE are available without charge from the Children's Bureau, Federal Security Agency, Washington 25, D.C. Copies may also be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D.C., at $.20 each, with the usual 10% discount on 100 or more copies.

# NEWS AND ANNOUNCEMENTS

Publication of the Academy's national report on the findings of the recently completed 2½-year study of child health services will be marked by a dinner on April 2nd in New York City, according to an announcement of Dr. Warren R. Sisson, President. A nationally known layman as well as an outstanding authority in medicine and public health are being invited to be guest speakers. The two-volume report which is now in press is being published by the Commonwealth Fund of New York.

* * *

SECOND PAN-AMERICAN CONGRESS OF PEDIATRICS, NOVEMBER 2-5, 1949

*Hospital Infantil, Mexico City, Mexico*

Plenary Sessions

Nov. 2nd. Acuate Diarrheas in Infancy; Hemolytic Syndromes of the Newborn.
Nov. 3rd. Congenital Malformations of the Heart; B.C.G. Vaccination in America.
Nov. 4th. Pediatric Surgery; Virus Diseases in Pediatrics.
Nov. 5th. Child Neuropsychiatry; Pediatrics in the Field of Social Security.

* * *

The University of Minnesota announces a course in Pediatrics to be presented at the Center for Continuation Study on April 7, 8, and 9, 1949. The course is intended for doctors specializing in Pediatrics. The first day of the course will be devoted to problems of allergy in pediatric practice. Emphasis will be placed upon diagnosis and management of hay fever, asthma, and skin allergy. Immunologic concepts will be emphasized, and an evaluation of the newer drugs will be presented. Two days of the course will be devoted to infectious diseases. Subjects to be presented include common respiratory diseases, toxoplasmosis, histoplasmosis, tuberculosis, and rheumatic fever. Faculty for the course will be made up of members of the staff of the University of Minnesota, Mayo Foundation, and distinguished visiting physicians from other medical centers.

* * *

A postgraduate course in Pediatrics will be given by the Department of Pediatrics, University of Arkansas School of Medicine, Little Rock, Ark., March 11 and 12. Topics of practical importance to practitioners will be discussed. Guest speakers will be Dr. James G. Hughes, Associate Professor of Pediatrics, University of Tennessee, Memphis, Tenn. and Dr. Myron E. Wegman, Professor of Pediatrics, Louisiana State University, New Orleans, La. Physicians are invited to attend. Notify Dr. William A. Reilly, Professor and Head-Pediatric Department, University of Arkansas School of Medicine, Little Rock, Ark.

* * *

The Rochester Child Health Institute has arranged for two fellowships, recipients of which will be called Assistants of the Institute. These assistantships last for one year, one beginning January 1, and one July 1, each year. The service is in *preventive medicine* in pediatrics and facilities including prenatal, newborn, infant, preschool and school care. Considerable emphasis is placed on psychiatric, psychologic, developmental and nutritional as well as the more purely medical supervision. The service can be arranged to allow time for research activities.

The American Board of Pediatrics gives credit for one year for training on this service. A stipend can be arranged for, ranging from $1600 up to $3600 according to previous training and dependents of applicant. Preference will be given to those anticipating teaching as their final goal.

Applications will be sent on request and should be submitted not later than nine months prior to beginning of service to Dr. Edith Hewitt, Chairman-Admissions Committee, Rochester Child Health Institute, City Hall, Rochester, Minn.

* * *

Dr. Samuel M. Wishik, former assistant director of the division of health services of the United States Children's Bureau in Washington, has been named head of the Health Department's recently

reorganized Bureau for Mothers and Young Children, Dr. Harry S. Mustard, Health Commissioner has announced.

In making the appointment, Dr. Mustard declared that his department's expanded program of services for the protection of premature babies and expectant mothers was "now well under way."

The new bureau director is a graduate of Columbia University and the College of Physicians and Surgeons. He did child health work in the Health Department from 1939 to 1942, when he was appointed senior assistant surgeon of the United States Public Health Service. He was assigned to Hawaii where he served both with the Public Health Service and the Hawaiian Board of Health in charge of maternal and child health.

During the poliomyelitis epidemic there in 1943-44, Dr. Wishik became medical director of the Emergency Poliomyelitis Hospital in Honolulu. As a consultant for the Children's Bureau, and State Department in 1946, he conducted a survey of maternal and child health problems in the Philippines. He is a past president of the American Academy of Pediatrics.

* * *

New officers of the Rocky Mountain Pediatric Society for 1949 are as follows: President, Dr. Wm. D. Rothwell, Jr.; Vice President, Dr. Mariana Gardner; and Secretary Treasurer, Dr. Edwin T. Williams.

Monthly meetings from October to June are held at the Children's Hospital in Denver.

* * *

The Medical Society of the District of Columbia presented a certificate for meritorious services to Dr. Joseph S. Wall at its recent meeting. Dr. Wall who was head of the department of pediatrics at Georgetown University School of Medicine, was cited for his outstanding contribution as a citizen and credited with having done more than anyone else for passage of the present Healing Arts Practice Act in the District of Columbia. He is a past president of the Society, and a past president of the American Academy of Pediatrics.

* * *

The 100th anniversary of the graduation of the first woman to receive a medical degree in the United States, Dr. Elizabeth Blackwell, was observed on January 23, 1949, in ceremonies at the New York Infirmary, 321 East 15th St., New York City, N.Y., and at Hobart and William Smith Colleges in Geneva, N.Y.

Here, five outstanding women doctors received the Elizabeth Blackwell citations for their contributions to medicine. In Geneva similar citations were awarded to 12 of the world's foremost women physicians in a colorful ceremony.

Those honored were: Dr. Priscilla White of Boston, for work in the field of treating diabetes; Dr. Florence R. Sabin of Denver, for medical research; Dr. Alice Hamilton of Hadlyme, Conn., for industrial medicine; Dr. Helen B. Taussig of Baltimore, for clinical medical research; Dr. Martha May Eliot of Washington, for public health; Dr. Gerty T. Cori of Webster Groves, Mo., for work in biochemistry and pharmacology; Dr. Helen V. McLean of Chicago, psychiatry; Dr. Margaret D. Craighill of Topeka, Kan., for military medicine; Dr. Helen MacMurchy, C. B. E., of Toronto, child welfare and public health; Dr. Elise S. L'Esperance of New York, pathology and cancer prevention work; Dr. Theresa Bertrand Fontaine of Paris, first French woman medecin des hospitaux.

At the local observance Mrs. Frank A. Vanderlip, president of the board of trustees of New York Infirmary, presented the citations to four of the physicians chosen. Dr. Ada Chree Reid, a member of the Metropolitan Life Insurance Company's medical staff and chief of the cardiac clinic of the New York Infirmary, was absent because of the death of her mother.

The four who were present were: Dr. Lauretta Dender, senior psychologist-in-charge at the children's service of Bellevue Hospital and associate professor of psychology at New York University Medical School, for her achievements in child psychiatry; Dr. Connie Myers Guion, chief of the medical clinic, out-patient's departments, New York Hospital, and associate professor of clinical medicine at Cornell Medical School, for her work in internal medicine; Dr. Anna Hubert, director of the department of surgery and gynecology of the New York Infirmary, for surgery; Dr. May G. Wilson, chief of the pediatric cardiac clinic of New York Hospital and associate professor of clinical pediatrics at Cornell University Medical College, for pediatric cardiology.

# BOOK REVIEWS

CONGENITAL MALFORMATIONS, Douglas P. Murphy, M.D., 2nd edition. $5.00, 128 128 pages. J. B. Lippincott, Philadelphia 5, Pa., 1947.

Dr. Murphy has attempted to answer two very important questions: what causes congenital defects and what are the chances confronting porspective parents, particularly if they have already had one defective child? The first edition of his book published in 1940 set forth the genetic factors as they occurred in a group of nearly 900 defective children studied by him and his collaborators. The second edition is not an extension or revision of these former observations, but simply adds two chapters dealing with two environmental factors responsible for congenital defects. These added chapters deal with the effects of pelvic irradiation and maternal rubella on the fetus.

By limiting himself to these two factors the author has left out of consideration any reference to several other important environmental factors, including maternal diabetes, maternal diets, toxoplasmosis and the Rh factor. The book also gives rather limited answers to the two important questions posed by Dr. Murphy by virtue of the fact that the definition of congenital malformations is restricted. No information is given concerning the inheritance or acquisition during fetal existence of many specific defects, such as blindness, deafness, mental deficiency and many other less frequent but important malformations. Such a book is needed and it is hoped that Dr. Murphy's great interest in the problem will lead him on to an extension of the work he has begun.

HERBERT C. MILLER

HUMAN EMBRYOLOGY, Bradley M. Patten, Professor of Anatomy in the University of Michigan Medical School. $8.00, 776 pages, 1366 drawings and photographs. The Blakiston Company, Philadelphia, 1947.

In his preface Dr. Patten says, "This book represents an endeavor to set forth in simple and readable form the phases of human embryology which are of special interest to medical students and physicians." When one has read this book carefully, with enjoyment of the clarity of both illustrations and text, one can say with considerable enthusiasm that Dr. Patten has been successful in his endeavor. Very few student texts in the basic sciences make such good leisure time reading for the pediatrician. It is both beautifully and ingeniously illustrated, many of the drawings being Dr. Patten's own. Even if the busy pediatrician is not stimulated to read the book through, he should be aware of its great value as a reference source to aid him in understanding many of the abnormalities seen in early infancy.

The arrangement of the text lends itself to both easy reading and convenience for quick reference on a specific problem. The first four chapters deal with the general background of knowledge needed to understand the development of the human embryo and carries the reader through the first establishment of the embryonic body. The third and fourth chapters are especially pleasing in their clarity of presentation of such difficult subjects as fertilization, cleavage, the formation of germ layers, and the general structure of the early human embryo. Chapters five through eight present the total picture of embryonic development through its first six weeks of existence. This enables Dr. Patten to give a description of the differentiation of the body and the establishing of organ systems which holds the reader's attention as well as an absorbing novel. Following the eighth chapter on "Twins, Double Monsters and Teratology" Dr. Patten goes back to take up thoroughly and systematically the development of each system through the whole embryologic and fetal life.

Among these 11 chapters those on the bony skeleton, the nervous system, and the heart and circulation stand out as unusual examples of clear exposition. Dr. Patten's gift for combining excellent drawings with unusually lucid description stimulates the reader to use logic rather than mere memory in mastering the subject of human embryology. And, finally, each of these chapters contains references to abnormalities which result when the orderly process of development is disturbed by either genetic or environmental factors. This helps to give pleasant motivational stimulus to the student, and enhances its value as a reference work for the pediatrician.

PHYSICAL FITNESS APPRAISAL AND GUIDANCE, by Thomas Kirk Cureton, Jr., Ph.D., M.A., M.P.E., assisted by Frederick W. Kasch, B.S., M.S., John Brown, B.S., and W. G. Moss, Ph.D. First edition, $6.00, 566 pages with 129 illustrations, C V. Mosby Company, St. Louis 3, 1947.

Professor Cureton and his associates in physical education at the University of Illinois present in this volume a wealth of information and experience in the field of estimating physical fitness. Certainly welcome at any time, the book is especially appropriate now when interest in positive improvement of health, i.e., fitness, is increasing. Total fitness, of course, implies more than freedom from physical disease or disability; and omission of sections on mental, social and emotional fitness is recognized by the authors early in the book. This volume comprises a review of the literature on testing physical fitness, an analysis of 22 tests for appraisal of physique, organic efficiency and motor efficiency applied in 1945 to 110 first-year medical students and the use of test results in health counseling. Attention is focused on the challenge to improve the health of supposedly normal individuals.

Chapters have such titles as "The Appraisal of Body Type as an Approach to Health and Fitness Guidance," "Appraisal of Physical Fitness by Pulse Rate Tests," "Respiratory Fitness," "Strength as an Index of Fitness," and "Motor Fitness Tests as Measures of Fitness." Chapter 10, "Physical Fitness Problems Related to Strenuous Exertion," will appeal to pediatricians especially because of its extensive review of evidence and opinions on good and bad effects of hard exercise at all ages. Most experts believe that young persons suffer no damage, cardiac or other, from strenuous exercise. The chapter is a valuable reference for those who must plan or advise on activity programs for children.

Chapter 8, "Rating Cardiovascular Condition by the Heartometer Pulse Wave Tests," is disappointing because extravagant claims made for the information gained from minute analysis of arteriograms ("heartograms") are not documented by published data.

Most physicians will disagree with some of the opinions expressed in Chapter 15, "Principles of Health and Fitness Guidance." Undue and possibly dangerous emphasis is placed on the benefits of physical exercise, as for example in the following statement: "Quite likely, in most cases, the greatest majority of the chronic middle-aged ailments such as digestive upsets, heartburn, acidosis, postural diabetes *sic,* constipation, headaches, neurasthenia, fatty degeneration of the heart, breathlessness, chronic fatigue, piles, overweight, 'heart failure,' and kidney disorders would be greatly reduced if middle-aged adults followed a day by day program of two hours of physical work, preferably outdoors" (p. 492). A number of statements similar to this one reminds the reviewer that health guidance is still a medical matter.

In spite of obvious inadequacies which should be recognized by the critical reader, the book meets a definite need and is recommended reading because of the wide variety of tests the authors have described and analyzed. It will be especially rewarding for school physicians and nurses, selective-service examiners and, in fact, for all physicians who encourage periodic health examinations.

THOMAS E. SHAFFER

Pediatrics

VOLUME 3 MARCH 1949 NUMBER 3

# AMERICAN ACADEMY OF PEDIATRICS, INC. PROCEEDINGS AND REPORTS

## REPORT OF THE EXECUTIVE BOARD MEETING

### Atlantic City, N.J., November 17, 18, and 19, 1948

A meeting of the Executive Board of the Academy was held at Haddon Hall, Atlantic City, N.J., beginning Wednesday, November 17, 1948. It was called to order at 11:30 a.m. by the President, Dr. John A. Toomey. There were present Drs. Toomey, Sisson, Spickard, Munns, Barba, Pease, Stringfield, Hurtado and Grulee.

Applicants for membership were approved. (See list in Business Session Report.) The report of the President was read and accepted. The report of the Secretary was presented and accepted. (See PEDIATRICS 3:115, 1949.)

The Board recessed for luncheon at 12:36 p.m. and reconvened at 1:40 p.m. with the following additional members present: Drs. Martmer, McLendon (substituting for Dr. London) and McElhenney.

The report of the Treasurer was presented, discussed and accepted. (See PEDIATRICS 3:117, 1949.) The motion was made and carried that whenever possible the Annual Meeting be held in Chicago. The motion was made and carried that men elected to membership at the Executive Board meeting immediately preceding the Annual Meeting be considered members at the time of the Annual Meeting. The following District Reports were presented and accepted:

*District I:* All State Chairmen are working actively on the State Reports of our Study. Already the value of this Study is beginning to show itself. Dr. Root reports that some facts obtained from the Study in Connecticut are being used in the preparation of remedial recommendations in child care to the state. In Massachusetts Dr. Baty reports a complete survey of all health and welfare agencies is being made with the idea of revamping Boston's social structure. The Academy's Study for Massachusetts is being used to assist in this constructive work. The fellows of Rhode Island have elected and recommended for appointment Dr. Robert M. Lord to be their next State Chairmen. The fellows of Connecticut and Massachusetts are meeting early in November to discuss Academy affairs.

Respectfully submitted,

OLIVER L. STRINGFIELD, *Chairman*

*District II:* Work is being done toward the completion of the District II report of the Academy's Study of Child Health Services. Twelve fellows from this district have been added to our membership.

Respectfully submitted,

PAUL W. BEAVEN, *Chairman*

*District III:* The State Chairmen and Study Committees of the three states all report progress and expect to get their reports published this winter. One result of the Study has been to point out some of the inadequacies of pediatric education. At a meeting of State Chairmen on October 5, 1948, it was agreed that one thing to do at once is to stimulate state medical societies and state boards of examination and licensure to have separate examinations in pediatrics instead of a question or two in the examination on medicine. This has been started already in Pennsylvania through the action of the Committee on Child Health of the State Medical Society and the Pediatric Section of the State Society, both of which have sent recommendations to their respective superiors asking that such action be taken. This recommendation has been endorsed by the members of the Academy attending the meeting of the Pennsylvania fellows on October 5. It also has the endorsement of the Philadelphia Pediatric Society. In addition to this recommendation, it was suggested that some long range planning be undertaken to insure proper pediatric training of interns, as many hospitals accepted for intern training have an inadequate pediatric service for men who are to go into practice and have 35% of their work in the care of children. We hope this will result in a proper examination in the three states and ultimately in a better training program.

Respectfully submitted,

PHILIP S. BARBA, *Chairman*

*District IV:* All of the states in this district, which have not published their reports, have been active in making preparations for them and it is hoped that by the end of this year each state will have its own report in publication with proper recommendations. Items of special interest in the various states are:

Georgia: Active preparation is being made for the April Areal Meeting of the Academy in Atlanta. They hope to make this an outstanding meeting and the State Chairman has asked me to extend to all members of the Academy a most cordial invitation to attend. Members have also been active in advising with the State Health Department in the publication of the booklet, "Expectant Mothers and Child Care." The booklet was submitted before publication to the Academy membership for approval. There is close cooperation in Georgia among the Academy and the Georgia Pediatric Society, the State Medical Society and the State Board of Health, which has developed a very healthy situation for furthering child care in that state. Georgia's Child Health Service Report is about completed and is expected to be ready for distribution within the next month or two.

South Carolina: The Child Health Service Report is nearing completion and should be ready for publication in the near future. South Carolina pediatricians have had their state meeting, at which time two outstanding members of the Academy addressed the group: Dr. Waldo E. Nelson of Philadelphia and Dr. James L. Wilson of Ann Arbor.

District of Columbia: This group has experienced difficulty in preparing its Child Health Services Report because of the set-up of the fictitious state for purposes of comparison—with part of Maryland and part of Virginia showing along with the District of Columbia. This, however, is being straightened out and the report is coming along. Increased facilities for child care are being developed in Washington. The Children's Hospital is perfecting plans for a new structure; the City Hospital is about to begin construction for more adequate facilities for pediatrics, and Georgetown and George Washington Universities have completed and opened new hospitals, both of which have excellent pediatric facilities. It is worthy of note that in the George Washington University Hospital Maternity Department plans for "rooming-in" care for the newborn have been developed.

Maryland: Plans are being made to organize a Maryland Chapter of the Academy similar to that outlined by some of the other New England groups. Particular emphasis should be given to the work of the Premature Mortality Committee in Maryland, under the chairmanship of Dr. D. C. Wharton Smith, which has done an excellent job in cooperating with the National Committee on Fetus and Newborn. A detailed report of that will be given by the State Chairman.

North Carolina: Pediatricians have been active in implementing some of the recommendations made in their Child Health Services Report. A premature program has already been initiated in which there have been set up in the state six premature centers to provide adequate care for premature infants. This plan assures the infant adequate facilities in the premature nursery from the standpoint of equipment, nursing care, and supervision by trained pediatricians throughout their

stay. The Study Report has been widely distributed throughout the state, not only to the medical personnel, but to interested agencies who cooperated in the Study. Your Chairman had the privilege of explaining some of the results of the Study to the Governor's Committee on Child Welfare (Division of the White House Conference) at its meeting in September. Representatives of the Academy met with the state orthopedists and the State Board of Health and aided in working out a plan for the follow-up care of patients who had poliomyelitis during the epidemic of 1948.

Respectfully submitted,

ARTHUR H. LONDON, JR., *Chairman*

*District V:* The State Chairmen have been busy working on their reports for the Child Health Study and expect to have them ready in the near future. In Kentucky the postgraduate course in pediatrics at the Children's Hospital was given this year with good and enthusiastic attendance. In Ohio Dr. J. Victor Greenebaum, State Chairman of the Committee on Fetus and Newborn, and Dr. Susan Souther of the Children's Division of the State Department of Health have been working on standardization of procedures for the nurseries in maternity hospitals. An effort is being made among pediatricians in Ohio to stimulate interest in accident prevention.

Respectfully submitted,

JAMES W. BRUCE, *Chairman*

*District VI:* The Mid-west Areal Meeting was held in Milwaukee, Wis. on June 28, 29 and 30. A total of 530 members and guests registered. The entire program was arranged by the Academy fellows of Milwaukee and they are to be congratulated for providing a meeting which was most instructive, interesting and satisfactory to everyone present.

Reports of Academy activities from four states have been received: Dr. Goldie E. Zimmerman from South Dakota reports that the state Study and report have been completed. Dr. James E. Dyson of Iowa reports that a meeting of the Iowa Pediatric Society was held in conjunction with the State Medical Society's Annual Meeting. A second meeting is planned for October at Iowa City in conjunction with a two-day graduate session. Premature centers are being planned in Des Moines, Sioux City and Iowa City under the guidance of the State Committee on Fetus and Newborn. Dr. Lee F. Hill heads this Committee. The other members are Drs. Robert H. McBride and Robert Johnson. Arrangements have been made to publish the Child Health Services Report in the *Iowa State Medical Journal* during this winter.

Dr. Ralph E. Dyson of North Dakota reports that all Academy fellows met in conjunction with the State Medical Society and plans were formulated to organize a state pediatric society. General practitioners who have particular interest in the care of children will be invited to join this group.

Dr. Eugene T. McEnery reports from Illinois that the Academy is cooperating with other organizations interested in child welfare in laying plans for the White House Conference on Child Health which will be held in 1950. Dr. McEnery has also brought the Academy Child Safety Campaign to the attention of the State Medical Society.

Respectfully submitted,

GEORGE F. MUNNS, *Chairman*

*District VII:* Missouri: Kansas City has had a child guidance clinic for some time, and also a Rheumatic Fever Clinic at the City Hospital. Plans are going forward in two hospitals for Negroes in St. Louis to develop units for premature infants which will serve as teaching centers for both physicians and nurses. The Academy Study shows Missouri has two mental hygiene clinics in St. Louis and only eight other states had fewer visits to such clinics per 1000 children. St. Louis University group of hospitals have made considerable progress toward setting up an adoption code with a view to legislative action to prevent black market operations in this field. Visual screening tests are being undertaken for 12,000 school children through sponsorship of the Children's Bureau and National Society for prevention of blindness.

Alabama: Reports good support in collecting the data for the Study.

Louisiana: Academy activities in Louisiana are still centered around the Study of Child Health Services. An Editorial Committee consisting of Drs. Ralph V. Platou, Myron E. Wegman, W. C. Rivenbark, Verre Simpson and C. H. Webb is engaged in writing the State Report which will be published in the *New Orleans Medical and Surgical Journal* in serial issues, October, November and

December, 1948. Consultations have been held with a general advisory committee representing numerous other organizations interested in the field of child health.

The State Committee on Fetus and Newborn, Dr. Myron E. Wegman, Chairman, held its first meeting October 31, 1948, immediately preceding the quarterly meeting of the Louisiana State Pediatric Society.

Pediatric postgraduate and pediatric extension services will be carried out during the fall and winter months by the departments at Tulane and Louisiana State University, the extension work at the latter institution being under the direction of Dr. Sidney S. Chipmen, in cooperation with the Louisiana State Board of Health.

Texas: The Texas Committee for Children and Youth plans to use the Texas report of the Academy Study to help establish the needs of the children and youth of the state. There is some definite work being done and a very worthwhile program outlined which should be far reaching along these lines. The state is giving special attention to visual screening in our public schools throughout the state. Dr. Arild E. Hansen has been doing some very worthwhile work with refresher courses in the University of Texas Medical School, the most recent being held in Galveston November 8-13. We have Warm Springs Clinic in Gonzales which has been used very successfully for polio and other bone deformities.

Tennessee: Through the work of Dr. James Overall, Tennessee was the first state in District VII to complete the Child Health Services Report and actually put some recommendations to work.

Respectfully submitted,

THOMAS J. MCELHENNEY, *Chairman*

*District VIII:* The Western Areal Meeting of the Academy was held in Seattle, September 13-15. There were two days of scientific papers and one clinical session. One innovation on the program was a clinical pathologic conference presented by Dr. Francis Scott Smyth.

The State Chairmen's luncheon was attended by all except three state representatives. Discussion of Academy affairs showed that the State Chairmen were well informed on most problems facing pediatrics.

The membership in this District, at least, feel that any new policies recommended by the ICH Committee should be well publicized to the membership and have its approval. There is also the feeling that recommendations made from the Study of Child Health Services should be kept as near as possible to the state level and the state medical societies should be informed at all times about new policies of the Academy.

Respectfully submitted,

VERNON W. SPICKARD, *Chairman*

The following Committee Reports were presented and accepted:

## REPORT OF THE COMMITTEE ON COOPERATION WITH NONMEDICAL GROUPS

This Committee has completed its organization on a national basis. We now have representatives in every state and in all of the larger cities to deal with problems concerning P.T.A., Boy and Girl Scouts, Y.M. and Y.W.C.A. groups, camps, and other nonmedical groups. These sub-committee members have made many talks before the various groups as well as advising their medical committees and in many instances have done preschool examinations in the rural schools. In one or two states contacts have been made with United Mine Workers Health and Welfare groups. Although this type of work is carried on by the local sub-committee members, the National Committee deals with the national offices of these organizations. If any of the Academy members want to know their local or state committee members, the national committee member in their respective localities has this information.

The National Committee under the direction of Dr. Henry Utter is attempting to correlate the laws and regulations governing camps in the various states and to solidify and combine this information so that there will be a possibility of getting a national or uniform type of regulation. Dr. Utter hopes to have this work ready within another year.

The Committee also urges that the Academy members avail themselves of the camp card which was sponsored by this Committee and which we hope will become standard for all camps. Mead

Johnson & Company have plates and will distribute free of charge small quantities to the Academy members. There were about 300,000 of these used this past year.

The Committee is still pushing the use of the film, "When Bobby Goes to School," which has had wide distribution (also under the supervision of Mead Johnson & Company).

Respectfully submitted,

JAMES C. OVERALL, *Chairman*

## REPORT OF THE COMMITTEE ON FETUS AND NEWBORN

This Committee has completed a 50-page manual, "Standards and Recommendations for the Hospital Care of Newborn Infants—Full Term and Premature." This manual represents a revision of the preliminary manual presented last year incorporating many of the suggestions and criticisms received from fellows of the Academy as well as those from other interested groups and individuals. The manual is submitted to the officers and Executive Board at this time with the recommendation that it be given the official endorsement of the Academy.* Your Committee realizes that these standards and recommendations are not perfect and may not satisfy all. We solicit continuous criticisms of the material presented and assume the obligation of revising the volume from time to time as conditions warrant.

In preparing the manual we were informed that no Academy funds were available for publishing the manuscript. The Executive Board gave the Chairman authority to seek aid from outside sources. The Borden Company, Prescription Products Division, 350 Madison Ave., N.Y., through Dr. G. H. Wright generously came to the rescue and is publishing 1000 copies of the manual for us. While they will have a small credit line on the inside of the front cover of the booklet, this Committee would be grateful if the Executive Board would acknowledge our appreciation directly to the Borden Company by an appropriate resolution. The 1000 copies will only be sufficient to care for our present need of getting the manual endorsed as the official thought of the Academy and for distribution to members of the State Committees on Fetus and Newborn—but not enough for distribution even to the members of the Academy let alone the outside hospitals, individuals and groups requesting copies.

The State of New York has already placed an order for 375 copies and plans to put one copy in every nursery in the state. The Director of Hospitals for the Commonwealth of Massachusetts has expressed a similar desire to your Chairman. In Maryland as part of a program to educate general practitioners the Maternal and Child Welfare Committee plans to mail to all physicians delivering or caring for infants a copy of our manual when it is available in final form. This shows that there may be a general demand for copies of the manual. We would like an Executive Board decision as to whether (1) the Academy will publish the booklet or (2) the Committee on Fetus and Newborn shall arrange for private printing and distribution at cost.

The immediate objectives of this Committee—the preparation of a manual of standards and organization of state groups to implement these standards at local levels—are well on the road to completion. The directory of State Committees on Fetus and Newborn incorporated in the manual demonstrates the organization of the country into working groups. It is with great pride that we can report that, within one year of organization, the following State Committees on Fetus and Newborn have actually launched programs to improve some phase of newborn care: California, District of Columbia, Florida, Iowa, Kentucky, Maryland, Massachusetts, Michigan, Missouri, Montana, New York, North Carolina, North Dakota, Ohio, Pennsylvania, Texas and Washington.

Respectfully submitted,

STEWART H. CLIFFORD, *Chairman*

## REPORT OF THE PROGRAM COMMITTEE

The Program Committee suggests that at the San Francisco meeting ararngements be made to devote one-half day session to Infantile Paralysis and one-half day to the Care of the Handicapped Child. Any further suggestions concerning the program will be gratefully received and made available to the Program Committee appointed for 1949.

Respectfully submitted,

EDGAR E. MARTMER, *Chairman*

* Action on this recommendation was taken at a later session.

## REPORT OF THE COMMITTEE ON GEOGRAPHICAL DISTRIBUTION OF PEDIATRICIANS

Requests continue to come in for surveys of cities, counties, and regions including several states. I have made many of these surveys revising them up to 1947 and 1948. The men write that these surveys have been very helpful in their search for location for pediatric practice.

Respectfully submitted,

OTTO L. GOEHLE, *Chairman*

## REPORT OF THE COMMITTEE ON MOTHERS' MILK BUREAUS

The mothers' milk bureaus of the country still reflect in their activities the status of breast-feeding in general. This Committee, therefore, continues to regard as its main job the fostering of interest in and practice of breast nursing. A round table discussion has been arranged for the November meeting at Atlantic City—apparently the first time in more than 20 years of its existence that the Academy has discussed this fundamental subject at a national meeting.

The Committee continues to act as an information service assisting American and foreign workers in need of facts and opinions.

Respectfully submitted,

CLEMENT A. SMITH, *Chairman*

## REPORT OF THE COMMITTEE ON CARE OF EUROPEAN CHILDREN

The work of this Committee has been concerned entirely with the medical supervision of refugee children in cooperation with the United States Committee for the Care of European Children. In recent years the children examined by members of this Committee and its associates have been brought from Europe to the United States under the provisions of President Truman's Directive. In the period extending from May 20, 1946, to July 26, 1948, 1387 children have been examined at the Reception Center in New York City on the basis of this program. The President's Directive was terminated on June 30, 1948, and has been replaced by the new Displaced Persons Act. This legislation provides for immigration to the United States of 3000 orphan children under 16 on a non-quota basis. Those over 16 will be admitted on quotas of the countries of birth. Details of the plan under which these children will receive assistance and care are still in a negotiable state. It is not expected that new groups will be received in the Reception Center under the new act until some time in October. When they arrive medical examination will be resumed under the auspices of this Committee.

Respectfully submitted,

CARL H. SMITH, *Chairman*

## REPORT OF THE COMMITTEE ON TUMOR REGISTRY

A conference of the Committee members in New York City was held October 1, 1948. The following cases have been added to the Registry since the report of May 28, 1948:

| | |
|---|---|
| Retroperitoneal rhabdomyosarcoma | 20 months |
| Rhabdomyosarcoma of bladder | 8 years |
| Hematologic problem in twins | 3 months |
| Dermoid cyst of ovary | 9 years |
| Congenital epulis | newborn |
| Teratoid adenocarcinoma | 1 year |
| Neuroblastoma | 3 years |

Dr. Paul E. Steiner reports that the Committee on Tumor Terminology of the American Society of Clinical Pathologists, will remain inactive for the time being. It was discovered that there was a

great overlap in the interests of this committee and that of a subcommittee of the Committee on Pathology of the National Research Council. To avoid unnecessary expenditure of effort and funds, the American Society of Clinical Pathologists decided to keep its committee intact but inactive until the situation was clarified.

Dr. Roy R. Kracke has requested that, because of the multitude of his commitments, Dr. Roger D. Baker, Professor of Pathology, of The Medical College of Alabama replace him as a member of the Consulting Board of Pathologists of this Committee.

*Recommendation:* It is recommended that Dr. Baker be appointed a member of the Consulting Board of Pathologists of this Committee.

The assistance rendered the Children's Tumor Registry by the pathologists who compose our Consulting Board has been of inestimable value in our program. Appreciation of their efforts has been frequently expressed by the Chairman. These physicians are not members of the Academy and have given generously of their time and experience to assist us. It would seem that some official recognition by the Executive Board of the Academy would be a gracious mark of appreciation to these pathologists.

*Recommendation:* It is recommended that the Secretary of the Academy write to the various members of the Consulting Board of Pathologists of the Children's Tumor Registry and express the thanks of the Academy for their cooperation and aid.

It is requested that the Executive Board reconsider the recommendation approved June 26 concerning the preparation of a pamphlet for use of teachers, health workers, etc., on the subject of childhood cancer. The approval of the Board at that time carried with it the stipulation that funds for its printing and distribution were to be obtained from the American Cancer Society. Should the American Cancer Society find that funds are not currently available for such educational material the distribution of this publication must necessarily await a later decision on the part of the American Cancer Society.

*Recommendation:* Inasmuch as we believe that the Executive Board of the American Academy of Pediatrics found the proposed pamphlet acceptable in principle, it is recommended that this restrictive clause attached to the approval of the Board: namely, ". . . provided the funds were made available by the American Cancer Society," be removed from the statement of approval.

The Committee believes it would be of value to the Academy members to have the address of the Registry published monthly in the DIRECTORY SECTION of PEDIATRICS.

*Recommendation:* It is recommended that the Editor of PEDIATRICS be requested to include the address of the Registry in the DIRECTORY SECTION of that publication.

Colonel J. E. Ash, Scientific Director of the Army Institute of Pathology has communicated with your Chairman several times since our last report. Initially the establishment of a Children's Tumor Registry under the jurisdiction of the Army Institute of Pathology was proposed. At a subsequent conference in New York the present national character of the existing Children's Tumor Registry was explained. The feasibility of the establishment of a Registry of Juvenile Pathology in the Army Institute of Pathology was discussed. Your Chairman suggested that this proposal of Colonel Ash's be brought to the attention of the Executive Committee. A letter outlining the general purposes of such a registry was therefore sent to Dr. Grulee by Colonel Ash, and a copy of this received by the Chairman of the Committee.

The members of this Committee on Tumor Registry have been polled to ascertain their opinions of this proposal. Their replies will be submitted by the Chairman at the meeting November 18, 1948.

The organization of the Special Committee for the Study of Radiation Effects in Childhood is in progress. The Secretaries of seven national scientific societies have been notified of the action, June 26, 1948, of our Executive Board and it is expected that at least one meeting of the committee will be held before the end of 1948. The members thus far appointed are: George C. Andrews, Edith F. Quimby, Alfred Fischer, and Charles O'Regan.

The objectives of this committee were stated in our previous report. Any member of the Academy who has had experience of value, or questions pertaining to any phase of the study of radiation effects during childhood is cordially invited to communicate with me.

Respectfully submitted,

HAROLD W. DARGEON, *Chairman*

## REPORT OF THE NOMINATING COMMITTEE

*Recommendations:*

For Vice-President (President-elect):
Edward B. Shaw, San Francisco, Calif.
For District Chairmen:
District II—Paul W. Beaven, Rochester, N.Y.
District V—James W. Bruce, Louisville, Ky.
District VIII—Crawford Bost, San Francisco, Calif.

Respectfully submitted,

WARREN W. QUILLIAN, *Chairman*

## REPORT OF THE AMERICAN BOARD OF PEDIATRICS

### December 1947—November 1948

The American Board of Pediatrics has held four examination sessions: Philadelphia in January, Cleveland in April, Chicago in June, and Seattle in September. A total of 210 candidates were examined. Of that number 169 were certified and 40 failed. There is one more session scheduled for this year, at Atlantic City on November 17, 18 and 19, 1948. At this time 64 condidates will be examined.

Lists for the examinations scheduled for February in St. Louis, and April in Baltimore, have been filled for some time. The list for the examination next after that date is already more than half full.

Respectfully submitted,

JOHN MCK. MITCHELL, *Secretary-Treasurer*
HUGH MCCULLOCH
A. WILMOT JACOBSEN

## REPORTS OF REPRESENTATIVES TO NATIONAL ORGANIZATIONS

*American Camping Association*

Immediately after my appointment I wrote to the Secretary and Vice President of the American Camping Association offering the services of the Academy in matters of health in camp.

The American Camping Association has requested that, if possible, we make a survey of the laws relative to health, safety, and sanitation in our summer camps—organizational and private and that we make some effort from the health standpoint toward having these laws enforced. Some of this work I am doing now.

I have had numerous communications with people inquiring about various matters relative to camping and numerous requests for our health blank.

Camping in the last three or four years has become very much commercialized and the health aspect of many camps has been forgotten. Fees for matriculation at camp have been exorbitant and many unscrupulous people are establishing camps for the mere purpose of making money. This makes it all the more important that we make some efforts to have laws relative to good camping enforced. I understand that Dr. Overall is going to bring this matter before the National Committee of Co-operation with Non-Medical Groups.

Respectfully submitted

HENRY E. UTTER, *Liaison Officer*

*American Hospital Association, Council on Professional Practice*

The Committee for the preparation of a Manual on Procedures and Layouts for the Infant Formula Room, and the handling of formulas, held its concluding meeting in Washington, D.C., on September 25 and 26, 1948. Those comprising the Committee, sponsored and financed by the American Hospital Association, are as follows:

Dr. Russell A. Nelson, Assistant Director, Johns Hopkins Hospital; Dr. Marian M. Crane, Assistant Director of the Division of Research in Child Development; Mrs. Irene Waters West,

Dietitian, Presbyterian Hospital; Mr. Sidney M. Bergman, Director, Montefiore Hospital; Dr. Preston A. McLendon, Professor of Pediatrics, George Washington University School of Medicine; Dr. John Parks, Professor of Obstetrics and Gynecology, George Washington University School of Medicine; Miss Margaret A. Losty, R.N., Public Health Nursing Consultant; Mr. H. E. O. Heineman, Director, Research Development, Pet Milk Company; Dr. Anthony J. J. Rourke, Physician Superintendent, Stanford University Hospitals; Mr. Robert H. Miller, Mead Johnson & Co.; Dr. Hattie E. Alexander, Associate Professor of Pediatrics, College of Physicians and Surgeons, Columbia University.

Previous to this meeting several sub-committee meetings had been held in New York, St. Louis, Chicago and Washington. The results of these meetings were combined in a rough draft of the Manual setting up chapters on different phases of procedures from layouts of a formula room to the feeding of the infant. These chapters include recommendations for supervision, personnel training and examination of such personnel. The Committee recommends that a two room unit is desirable and suggestions are included for improving an existing one room unit. Procedures for bottle and nipple cleansing are given followed by step by step procedures for formula mixing. Terminal sterilization by autoclave (230°—7 lbs. pressure—10 minutes) or flowing steam (209-211° for 30 minutes) is recommended. Advantages and disadvantages are given for each method. These temperatures have been found sufficient to produce a clean formula as well as sterile nipple area when covered by a paper or metal (glass) cap. These temperatures and times have not destroyed the nutritive value of the formula as shown by experiments on ascorbic acid, thiamin and lycine values before and after heating. Cooling and storage, preferably in individual nurseries are described. Methods for warming the bottle and protection of the nipple just prior to offering to the infant are recommended. The problem of changing nipples in the nursery is discussed and is admitted to be a weak link in the feeding of the newborn. Plans are to set up a committee by the American Hospital Association to interest nipple manufacturers to improve types and quality of nipples.

The American Hospital Association proposes to set up in its Council on Professional Practice a reference library from which can be obtained plans for formula room construction and information concerning equipment and supplies. The Council of Professional Practice also will submit the final drafts of the Manual to the Academy for its approval.

Two problems are left unsolved by this Committee:

(1) The need for standardization of newborn formulas for hospitals. The committee suggested that I call the attention of the Academy to this and through the appropriate committee make such recommendations as they see fit.

(2) The Council of Professional Practice will communicate with the Academy, asking their cooperation in preparing a pamphlet on preparation and care of formulas in the home. The Committee was of the opinion that this was a subject which would be better handled by the Academy of Pediatrics.

Respectfully submitted,

PRESTON A. MCLENDON, *Liaison Officer*

*Children's Bureau*

As liaison officer of the Academy, I was invited to serve on the newly formed Advisory Committee to the Children's Bureau by Miss Katherine Lenroot. The purpose of the Committee is to advise the Children's Bureau on matters of policy affecting the programs for maternal and child health and crippled children's services. The Committee met on September 14 and 15, 1948, in Washington, D.C.

The Committee is composed of members of medical and allied organizations, lay organizations and some individuals, interested in the welfare of children, but not connected with any organization. Dr. Harry H. Gordon was elected Chairman of the Committee for three years.

The morning session of the first day was devoted to becoming acquainted with the work of the Children's Bureau as well as with the membership of the Committee. Dr. Martha M. Eliot and Dr. Edwin F. Daily gave a comprehensive review of the work of the Bureau.

In the afternoon two educational films were shown. The first film showed the care of the premature infant given at a premature station in Peoria, Illinois. The second film was entitled "Rheumatic Fever." This film stressed the convalescent care of the rheumatic child. Constructive

criticism of these films was made by several members of the Committee. One criticism was that the general practitioner was not given a sufficiently important role.

On the second day several matters of policy were discussed. A number of members stressed the importance of giving special emphasis to the school health program during the coming year.

The inadequate supply of medical and allied personnel to carry out a good national program for the maternal, child health and crippled children's services, and the ways and means of obtaining adequate personnel were discussed by the Committee.

No formal action on any matter of policy was taken.

At the next meeting the Children's Bureau plans to ask the committee to consider certain specific matters of policy and make definite recommendations.

The Committee adjourned after recommending that meetings be called by the Children's Bureau at least twice a year.

Respectfully submitted,

HARRY A. ONG, *Liaison Officer*

*National Foundation for Infantile Paralysis*

As Liaison Officer for the Academy to the National Foundation for Infantile Paralysis, I attended the meeting of the International Congress on Poliomyelitis held in New York in July.

This meeting lasted seven days and was devoted to speeches, conferences, demonstrations, etc. It was managed cleverly; all pertinent data about polio were covered and the demonstrations left little or nothing to be desired. The scientific exhibit was one of the best. The officers of this organization could be proud of their show.

We learned a great deal in the course of the days spent in New York, that would take many months to assemble and to digest. The report of the meeting will be the subject matter of a volume.

Respectfully submitted,

JOHN A. TOOMEY, *Liaison Officer*

*National Maternal and Child Health Council*

I have been told that the American Committee on Maternal Welfare has under consideration a mechanism for reviewing and classifying all books and articles dealing with infant and child nutrition. Does the American Academy of Pediatrics desire to become one of the organizations represented on this Committee?

The International and Fourth American Congress of Obstetrics and Gynecology will meet jointly at the Pennsylvania Hotel, New York City on May 14-19, 1950. Fifty-two American-Canadian and 42 foreign medical and allied Societies will participate. Does the Academy wish to participate? There will be no assessment.

Respectfully submitted,

MARGARET MARY NICHOLSON, *Liaison Officer*

* * *

The Secretary read a letter from Dr. Harold H. Mitchell, Academy representative to the National Advisory Committee on Local Health Units, recommending that the Academy consider a resolution favorable to the development of complete coverage of the United States by full-time local health departments, and enclosing a copy of a resolution adopted by the House of Delegates of the American Medical Association of June 10, 1942, as follows:

"Whereas, a major inadequacy in the civilian health protection in war as in peace time exists consequent upon the failure of many states and of not less than half the counties in the states to provide even minimum necessary sanitary and other preventive services for health by full time professionally trained medical and auxiliary personnel on a merit system basis, supported by adequate tax funds from local and state, and, where necessary, from federal sources: therefore, be it

"RESOLVED, that the Trustees of the American Medical Association be urged to use all appropriate resources and influences of the Association to the end that at the earliest possible date complete coverage of the nation's area and population by local, county, district or regional full-time modern health services be achieved."

The resolution was endorsed by the Board.

A letter was read from Dr. Archibald L. Hoyne, reporting on the two-day session of the

Subcommittee on Control of Communicable Diseases of the American Public Health Association. The report was received with thanks.

The report of the Historian was received, and Dr. Marshall C. Pease was given authority, upon motion regularly made and seconded, to proceed with the preparation of the History of the Academy.

The meeting adjourned at 5:30 p.m. to reconvene Thursday morning.

*Thursday, November 18*

The meeting was called to order at 10:05 A.M. by the President. The members present on Wednesday attended, with the exception of Dr. Hurtado. Other members of the Board present were Drs. Bruce and Bakwin—Dr. Bakwin substituting for Dr. Beaven. There were present, in addition to the Board, Dr. James Wilson and Dr. John Hubbard.

The report of the Committee for the Improvement of Child Health was received and accepted, with the following amendments to the summary:

Item 6 was changed to read: "In conformance with the action of the Executive Board taken at Dallas in December 1947, the ICH Committee is empowered to cooperate with committees dealing with all phases of child health when such requests have been approved by the Executive Board."

Item 7 was changed to read: "To recommend a committee to promote pediatric nursing education, as requested by the nursing groups."

Motion was made and seconded that the Fund Raising Committee of the Committee for the Improvement of Child Health be discontinued. Motion carried.

The motion was made and seconded that the President be empowered to appoint a committee to work with a committee from the American Medical Association, if it was found that such a committee was necessary.

The reports of the following committees were received and accepted:

## REPORT OF THE COMMITTEE ON STUDY OF CHILD HEALTH SERVICES

It is with a sense of gratification and some pardonable pride that we may report to the Executive Board that the Study of Child Health Services has been completed. A report under the title of Health Services for Children and Pediatric Education in the United States has already been submitted to you for your consideration. Many pertinent criticisms have been received and incorporated in a revised draft.

In accordance with authority voted by the Executive Board on June 26, 1948, The Commonwealth Fund was asked to undertake publication. This Fund, we are pleased to state, has accepted the report.

Despite the untiring efforts of our Executive Staff, it is impossible to anticipate publication before the first of next year, and possibly later. Conversations with other publishing houses indicated that the publication date would not have been advanced appreciably by having the report published commercially. Publication by The Commonwealth Fund is considered particularly favorable because of (1) the painstaking and thorough editorial revision given by their editorial staff; (2) publication at cost, resulting in a much lower price per volume; and (3) the prestige which Commonwealth Fund publications carry. It should also be noted that the Fund has agreed to contribute to the cost of preparation of charts which is considerable.

To date several state reports have been completed and others are in preparation. Progress in the preparation of state reports is indicated by the fact that in addition to the North Carolina report, copies of reports on the findings in Oregon, Mississippi and South Dakota are already in print and available for distribution. Those already reviewed prior to publication are Louisiana and Missouri. New York, Illinois, New Jersey and Colorado are in the process of preparation.

Reports and data on the findings of the study as published in medical journals have been issued in reprint form. These include the following four papers presened at the annual meeting of the Academy, Dallas, December 1947.

"Review of Private Practice: Pediatricians and General Practitioners"; reprint from PEDIATRICS, March 1948.

"Total Volume of Medical Care for Children"; reprint from PEDIATRICS, February 1948.

"Impressions of Pediatric Education"; reprint from PEDIATRICS, April 1948.

"The Committee for the Improvement of Child Health"; reprint from PEDIATRICS, May 1948, and in addition:

"Community Health Services for Children in Eight Selected States"; reprinted from the *American Journal of Public Health,* January 1948.

"Health Services for the Rural Child"; reprint, *Journal of the American Medical Association,* May 22, 1948.

"Child Health Services in North Carolina"; supplement to *North Carolina Medical Journal,* April 1948.

"How Well Does North Carolina Provide for the Health of Its Children?"; non-technical version of the North Carolina report.

In respect to the final accounting of the Study of Child Health Services, the grant from the National Foundation for Infantile Paralysis was expended as of March 31, 1948, and a final accounting was made and approved by the Foundation. The grant from the National Institute of Health was expended as of June 30, 1948. The books were audited, approved and closed by a government auditor on this date. The third account, which has been designated as the "Academy Account," has a remaining balance of approximately $1800 which was set aside to cover a commitment made for the graphic work involved in the national report. Since now it appears likely that this expense will be covered, at least in part, by the Commonwealth Fund, any balance which may remain in this account when the Study Committee ceases to exist will be returned to the office of the Treasurer to be applied against the amount of $3000 borrowed from the funds of the ICH Committee.

The offices in Washington were closed July 28. Furniture and equipment belonging to the two bureaus of the government were returned, the remaining equipment and furniture being moved to the offices of the ICH Committee at The Children's Hospital in Philadelphia.

Since now the assignment for which this Committee was created has been finished, or will be shortly with the publication of the report, it is recommended that the Committee be discontinued on or about the date when the publication is released.

We wish to take this opportunity to express our sincere appreciation to all those who have made this vast undertaking possible and who have labored wholeheartedly to bring this undertaking to a successful completion. It would be impossible to name all those who have participated in the Study. However, we wish to express our particular thanks to Dr. Martha Eliot and Dr. Thomas Parran for their support and for having assigned to our Executive Staff personnel without whose experience and technical ability this Study could not have been accomplished.

Special credit is due to the Academy Chairmen who have carried the responsibility of organizing and conducting the Study in their own states. Just as at the national level, so also among the states, the Study has been conducted as a cooperative project in which medical, pediatric, and dental societies and other official and voluntary health agencies have participated.

For the generous financial aid which the Academy has received to meet the cost of the Study, we are indebted to the National Foundation for Infantile Paralysis, the National Institute of Health of the U. S. Public Health Service, The Field Foundation, Independent Aid, Inc. and the following commercial houses: Mead Johnson & Company, Pet Milk Company, Carnation Company, M & R Dietetic Laboratories, Borden Company, Lederle Laboratories, and the National Dairy Products Company, Inc. Many of these and others have given to the continuing ICH Committee and due acknowledgement and appreciation will be shown in the future reports from that Committee.

The cost of collecting the desired information in the states was met in various ways. Contributions were received from County Chapters of the National Foundation for Infantile Paralysis, state departments of health, state and county medical societies, and other sources with special regional interests.

It must be realized that the function of the Study Committee has been to report the findings of the Study. However, it is worthy of note that an analysis of these findings has already been made by the ICH Committee and specific recommendations for an action program will be found in a report of that Committee dated September 29, 1948, and submitted to the Executive Board.

Respectfully submitted,

JOHN P. HUBBARD, *Director*
WARREN R. SISSON, M.D., *Chairman*

## REPORT OF THE COMMITTEE ON LEGISLATION

Available to all is knowledge that Mr. Oscar R. Ewing, Chairman of the recent National Health Assembly, has interpreted data so derived to mean that there is an urgent need for legislation which would place the practice of medicine directly under federal control. Through a form of socialized practice the annual death toll will be "reduced" and the economic difficulties of the populace in gaining "adequate" medical care will be abolished by the simple expedient of spreading the load through taxation. This Truman-Ewing legislation we believe has little chance of acceptance at this time. Mr. George J. Hecht of the American Parents Committee has tentative draft of a bill it is proposed to introduce, "National Child Research Institute Act." Request has been made by Dr. John P. Hubbard to allow publication in PEDIATRICS. Careful study of this proposed Act will be made, with a watch kept on its progress. Views of members of the Academy will be welcomed.

Respectfully submitted,

COURSEN B. CONKLIN, *Chairman*

The meeting recessed at 12:30 P.M. to reconvene at 5:00 P.M.

The meeting reconvened at 5:00 P.M. Present, in addition to the Board Members, were Drs. Margaret M. Nicholson, Stewart H. Clifford, James M. Baty and Harvey E. Garrison.

It was moved and seconded that Dr. Margaret Nicholson obtain further information on the American Committee on Maternal Welfare and the advisability of the Academy's becoming one of the organizations represented on that Committee. Motion carried.

Motion was made, seconded and carried that the Academy officially endorse the Manual on Standards and Recommendations for the Hospital Care of Newborn Infants—Full-term and Premature. It was moved, seconded and carried that the Manual be distributed in planographic form to anyone asking for it at a fee to be determined.

The meeting recessed for dinner at 5:40 P.M. and reconvened at 7:00 P.M.

Motion was made, seconded and carried, that in each issue of PEDIATRICS, in the heading of the special news letters in the Correspondence Column there should be a statement that "The opinions expressed herein are those of the writers and are not an official expression of opinion by the Academy."

The report of the Committee on Reorganization was presented:

## PRELIMINARY REPORT OF THE COMMITTEE ON REORGANIZATION

We are agreed that there should be an organization of the members of the Academy in the individual states ("states" as used in this letter include provinces and Latin American countries) where there are resident ten or more fellows of the Academy. This will involve the addition of a separate section in Article III of the By-Laws stating that such organization is to be effected and further that this organization is to have at least one annual meeting, I should think within one month of the Annual Meeting of the Academy, and that the elected president of the state chapter be appointed the state chairman. This will also necessitate a clarification of the appointment of the state chairmen in states in which there are less than ten members.

The second suggestion for change that we are all agreed upon is the election of the district chairman by the members of the district which he represents rather than his election by the fellows from the entire Academy at the annual meeting. This will involve a change in Article I, Section 8, and a change in Article II, Section 3. It would seem logical to have the state chairmen of the districts act as a nominating committee for the district chairman and alternate district chairman. It would seem logical that the alternate district chairman should be elected in the same way as the district chairman. This latter will involve a change in Article III, Section 2 A.

The other point which would not seem controversial is the clarification of Article VII whereby "emeritus fellows" would receive the fellowship list and other publications of the Academy without charge.

There are certain other questions which I doubt we will be able to clarify before we get together as a committee.

The most important of these is the establishment of a "House of Delegates." Most of us and most of the other fellows including officers with whom I have discussed the problem have agreed

that if we make the above changes in the organization that this will not be either necessary or practical. At any rate we can discuss this more fully at our meeting.

Another question which we have not discussed is whether our Committee should attempt, with the help of the Committee on Legislation, to rewrite the entire By-laws to include our recommendations and rearrange the different articles and sections in more logical sequence.

Another matter which should be discussed is whether our Committee should make suggestions for changes in an effort to clarify the functions of the two branches of the Academy: one, Executive; two, Research. It has been suggested that this would lead to a more efficient organization of the Academy as a whole and in particular would clarify the functions and responsibilities of the different special committees. Some such clarification will obviously have to be done at some time; the question is whether now is the best time. I think we should explore this idea rather fully.

The only other point which I have thought of is whether we should make a suggestion that Article XI, Section 2, be changed. With 11 members of the Executive Board, it seems that four is a rather small quorum for the transaction of business. Six would be a better number so that a minority of the Executive Board would not be allowed to transact important business.

Respectfully submitted,

JAMES M. BATY, *Chairman*

The following amendments to the By-laws were approved by the Board:

Page 7, Article I, Sections 8 and 9 would read:

"*Section 8. Duties of Nominating Committee.* The duties of the nominating committee shall be to nominate candidates for the elective office of Vice-President. In case of any contingency arising whereby the Vice-President (President-Elect) is unable to fulfill the duties of that office, the Executive Board, on recommendation of the Nominating Committee, shall be empowered to appoint his successor.

"*Section 9. Notification of Nominations.* The list of nominees for Vice-President shall be submitted to all of the fellows in writing at least one month before the annual meeting, and the election of all nominees shall be by a majority of all the members voting at the annual business meeting."

Page 8, Article II, Sections 1 and 3 would read:

"*Section 1. Number.* The Executive Board shall consist of the President, Vice-President, and one member from each of the districts of which the Academy is composed, who shall be designated as the District Chairman. The District Chairmen shall be elected by ballot by the Fellows of the Academy residing in their respective district as hereinafter provided."

Section 2 to be left as it is.

"*Section 3. Subsequent Elections.* Each year successors to the District Chairmen shall be elected for a term of three (3) years from the Districts the term of whose Executive Board members shall have expired. No member shall serve for more than two succeeding terms.

"*Section 3a. Method of Election.* The State Chairmen of each district shall constitute a 'District Nominating Committee.' The President shall designate one member of each committee as chairman.

"Three (3) months before the expiration of the term of office of a District Chairman, the Nominating Committee of that district shall present to the Secretary the names of one or more nominees for the office. The Secretary shall mail a ballot showing these nominations to the fellows residing in the District concerned. The marked and signed ballots must be returned to the Secretary one (1) month before the annual meeting for tabulation. The results of the elections shall be certified by the Executive Board.

"The Secretary shall announce the results of these elections in the official Journal and at the Annual Meeting.

"In case of any contingency arising whereby any District Chairman is unable to fulfill the duties of that office, the Alternate District Chairman shall become the District Chairman.

"In case of any contingency arising whereby any Alternate District Chairman is unable to fulfill the duties of that office, the President shall appoint his successor."

Section 4 to remain as it is.

The heading of Article III would be changed to "Powers and Duties of the Executive Board, District Committees and Chairmen of States and Territories of the United States, the District of Columbia, the Provinces of Canada, and the Countries of Latin America."

Sections 1 and 2 of Article III to remain as at present.

Section 2a to be changed as follows:

"*Section 2a. Alternate District Chairmen.* Alternate District Chairmen shall be elected by ballot by the fellows residing in their District in the same manner as the District Chairmen (see Art. II, Section 3a). Each Alternate District Chairman shall serve for a term of three years and not serve more than two succeeding terms. To put this plan into effect the Alternate District Chairmen for Districts I, IV and VII shall serve for three years, for Districts II, V and VIII for one year, and for Districts III, VI and IX for two years."

Section 3 to remain as it is.

Add the following to Section 4:

"The Alternate District Chairmen are privileged to attend all meetings of the Executive Board as observers."

Section 5 would be rewritten as follows:

"*Section 5a. Organization of Fellows.*

"A chapter shall be established in each state and territory of the United States, the District of Columbia, each Province of Canada and in the countries of Latin America.

"*Section 5b.* The membership of each chapter shall consist of such fellows, whether active or retired, as have legal residences within the boundaries of the state.

"*Section 5c.* Each chapter may elect officers and adopt by-laws and regulations for the government of its own affairs and levy assessments, provided such by-laws and regulations are not in conflict with those of the Academy.

"*Section 5d.* The Academy shall be represented at the state level by one or more state chairmen who shall be elected for terms of three (3) years by vote of the fellows of that state. The number of such representatives shall be determined by the Executive Board.

"*Section 5e.* The present state chairmen shall continue in office until their successors have been elected.

"*Section 5f.* In the event that a representative is not elected within a period of one year after the adoption of these by-laws, the President shall appoint a state chairman after consultation with the District Chairman."

The only other change is in Article XI, Section 2, changing the requirement for a quorum from four to seven, the section to read:

"*Section 2. Quorum.* Seven members of the Executive Board shall constitute a quorum for the transaction of business."

Motion was made, seconded and carried, that the Reorganization Committee headed by Dr. Baty be continued.

The meeting adjourned at 8:30 P.M. to reconvene at 9:00 A.M. Friday morning.

*Friday, November 19*

The meeting was called to order at 9:10 A.M. by the President. There were present, in addition to the Board, Drs. Hugh McCulloch, Frank H. Lancaster, John K. Glen, Roger Kennedy, Harold W. Dargeon and George M. Wheatley.

## REPORT OF THE EDITORIAL BOARD OF "PEDIATRICS"

This report covers the first year of publications of PEDIATRICS. Many of our early plans were speculative, since no precedents had been set. However, the high standards set at the beginning have been maintained and the procedures for carrying them out have been developed. Policies continue to be established as we better the coordinaton of the journal's six widespread centers of operation: the Editorial Board, the Editorial Office, the Academy office, the Publication Committee, the Publisher and the Printer. Meetings with the Editorial Board, the Publication Committee and the Executive Board during the year have aided greatly in defining duties and responsibilities as well as determining policies.

As we review this first year, the publication speaks for itself to a large extent. The format was carefully planned and now is approaching final form. Cover stock weight and color are not as planned, but are the best available at present. As soon as paper supply is more plentiful, a more desirable stock will be used. And when printing facilities are available, it is planned to have the

page printed in double column. The shorter necessary eye-span will make for easier reading. When this change is made, the type face also will be made less condensed so that the printed page will carry fewer, better spaced words. At present there are many more words per page than most medical journals carry. The Editorial Board will seek constantly to improve the format as opportunities arise, and will make changes as fast as they seem necessary and desirable.

The labor of getting a new publication started is great, as is to be expected. The machinery of editing, publishing and printing is complicated and requires time and actual operation to perfect. PEDIATRICS' machinery is now working smoothly and, we believe, efficiently. There has been a natural difficulty, requiring extra time, arising from the separate location of the various groups concerned with publication. The elements of time and distance have been, for the most part, overcome.

The present status of the journal is good. It is on schedule, and no further difficulty in timing is anticipated. At present an ample supply of manuscripts of good quality is being received. It is planned that all manuscripts accepted will be published no later than six months after date of receipt —and in most instances sooner. The quality of PEDIATRICS, like that of every other medical publication, is determined by the quality of the Original Articles which are accepted. The Editorial Board has set very high standards for this division. Its content is as varied as the field and interests of pediatrics itself. Each manuscript is examined by at least two members of the Editorial Board; if there is a difference of opinion further reviewing is done. Some papers are referred also to persons not on the Board who have special knowledge of the subject, either to the chairman of an Academy committee or occasionally to someone who is not even a member of the Academy but is an expert on the subject involved.

Academy affairs are an important part of PEDIATRICS. Proceedings and reports are published and the journal is beginning to function as a forum for discussion of both Academy activities and all other matters of pediatric interest as well. The President has announced that contributions of this sort will be received and the Editorial Board is eager to include relevant letters and comments. Comments on original articles are particularly desirable, inasmuch as they often concern subjects about which there may be natural differences of opinion. In this case correspondence should be helpful and stimulating.

PEDIATRICS' financial status has improved and should continue to do so, as the Publication Committee's report will bring out. Efforts to increase advertising and subscriptions are being made, and a special subscription rate has been put into effect for residents and students.

The Editorial Board looks with confidence to the future of PEDIATRICS. There is every reason to believe that aims and ideals are being attained and that the journal should not only serve pediatrics the world over, but also be an important source of income to the Academy. We hope all members of the Academy will aid in accomplishing these purposes. The Board is receptive to suggestions and is appreciative of the assistance and support which has been rendered from many sources this past year. This support has made the task a pleasant one.

Respectfully submitted,

HUGH MCCULLOCH, *Editor-in-Chief*

The report of the Editorial Board was received and accepted.

The report of the Publication Committee was received and accepted.

## REPORT OF THE COMMITTEE ON RHEUMATIC FEVER

This report to the Executive Board covers the work of the Committee for the period February through September 1948. The Committee's work for 1947 was described in a special report published in PEDIATRICS, 1:528-530, 1948.

### *Rheumatic Fever and the School Child*

The statement "Rheumatic Fever and the School Child" prepared jointly by the Committees on School Health and Rheumatic Fever as a guide for school health authorities was published in PEDIATRICS, 2:321-323, 1948. Reprints of this have been obtained and will be distributed as widely as possible to school and public health authorities throughout the country. It is the desire of the two Committees to have state chairmen bring this to the attention of school health authorities in their respective states. This can be discussed with the state chairmen at the time of their meeting in Atlantic City.

*Film on Diagnosis of Rheumatic Fever*

The motion picture script has been completed for the film on the diagnosis of rheumatic fever. The title is "Is It Rheumatic Fever?" The script has been reviewed several times by the Committee members and by other authorities in the rheumatic fever field. They all seem to be highly satisfied with the script which is now ready to be made into a motion picture.

*Study of Rheumatic Fever Programs*

The Executive Board at the request of the Chairman of this Committee authorized the Committee to explore ways and means of establishing a project to carry out the Committee's recommendation that state and local rheumatic fever programs be reviewed and evaluated. The Chairman has discussed this with Dr. Martha Eliot, U.S. Children's Bureau, and can report that she would welcome a study of the state programs.

The project has been brought to the attention of the Executive Committee of the American Council on Rheumatic Fever at a meeting held September 22 in New York. The Executive Committee of the Council was in accord with the idea of the evaluation of state programs and indicated that the Council should take some responsibility for this inasmuch as the Council has a committee to prepare standards for community programs. The Council took no formal action but showed its readiness to secure funds for such a project.

The problem was also discussed at the meeting of the ICH Committee of the Academy, and this Committee is also desirous of assisting with this study.

The Chairman believes that the Study should be a joint undertaking of the American Council on Rheumatic Fever and the Rheumatic Fever Committee. If funds can be obtained, it is logical to expect that these would come through the Rheumatic Fever Council.

*American Council on Rheumatic Fever*

The Executive Committee of the Council met on September 22 to consider the relationship of the Council to the American Heart Association, in view of the Association's reorganization. A special committee of the Council was designated to prepare a statement which would define more clearly the relationship of the Council to the reorganized AHA. As yet, no allocation of funds obtained by the AHA from the Walking Man contest has been made to the Council. The Council itself obtained $25,000 through a special radio program conducted by Paul Whiteman in April 1948. The Council is financing two research fellowships both concerned with the study of mesenchymal tissue in relation to rheumatic fever. These fellowships are made possible by contributions from the American Legion. The Council has three immediate projects: 1. Production of a primer on diagnosis and treatment of rheumatic fever. 2. Developments of standards for community programs. 3. Establishment of policies and procedures for research. It was agreed that funds should be spent to obtain a staff to activate these two latter projects. Dr. David Rutstein, Professor of Public Health, Harvard University, will prepare the primer on diagnosis and treatment.

At this meeting, it was announced that the American Rheumatism Association was seeking funds through a newly established organization known as the Arthritis and Rheumatism Foundation. This Foundation intends to use the appeal of the child and rheumatic fever to raise funds. A drive will be launched in November. There was concern expressed that this new fund-raising effort would confuse the public especially in terms of rheumatic fever. A recommendation was prepared to the Executive Board of the AHA suggesting that the delegates from the AHA confer with representatives of the American Rheumatism Association to work out a method of operation which would minimize or eliminate this.

Respectfully submitted,

GEORGE M. WHEATLEY, *Chairman*

The report of the Rheumatic Fever Committee was received. Motion was made, seconded and carried, that the Committee be authorized to work in conjunction with the Rheumatic Fever Council. The Committee was authorized to formulate plans and explore sources of funds, following which it is to report back to the Executive Board in June. Upon motion regularly made and seconded, the report of the Committee was accepted with thanks.

The supplemental report of the Committee on Tumor Registry was received and accepted.

Motion was made, seconded and carried, that Dr. Dargeon select the men he wishes to have serve with him on an investigating committee and report back to the Board.

Motion was made, seconded and carried, that the Secretary be authorized to plan an area meeting for the Bellevue-Stratford Hotel at Philadelphia in 1950.

The following Alternate District Chairmen were elected:

District 3—Harold A. Murray

District 5—Benjamin Hoyer

District 6—Roger Kennedy (Subject to approval of State Chairman)

District 8—Frank Douglass.

The meeting recessed at 12:00 noon and reconvened the same evening, at 7:15 P.M., with the following people present in addition to the members of the Executive Board: Drs. Bret Ratner, Milton J. E. Senn, and James G. Hughes.

The report of the Section on Allergy was given by Dr. Ratner, and upon motion regularly made and seconded was accepted.

Dr. Senn presented the report of the Committee on Mental Health as to the progress in the establishment of a Section on Mental Health and Mental Hygiene. Motion was made, seconded and carried, that the report be accepted as a progress report.

The report of the Committee on Cooperation with The American Legion was presented by Dr. Hughes. The report was accepted.

The following resolution was approved:

"The Chairman of the Committee on Hospitals and Clinics, having canvassed the pertinent experienced colleagues, recommends to the Executive Board that it approve that the Committee on Hospitals and Clinics go on official record as advocating physically separate pediatric units as the desired form of proper pediatric hospital care."

Ten fellows were accepted as Affiliate Members in Surgery (see Report of Business Session). The meeting adjourned at 8:50 P.M.

# SEVENTEENTH ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

## BUSINESS SESSION—PRESIDENT JOHN A. TOOMEY PRESIDING

President Toomey: The first matter to come up is the report of the Secretary.

Dr. Grulee: My printed report has been handed to you as you came in the door. I am not going to read this report. An addition to make to it is that a special meeting of the Executive Board of the Academy was held at 4:30 P.M. Sunday afternoon, November 21, 1948 at Haddon Hall, Atlantic City. President Toomey presided. At this meeting the motion was made, seconded and carried that Dr. Sisson and the Committee he may select be empowered to explore the possibilities of publicizing the Academy's Study of Child Health Services, with absolutely no power to act except by approval of the Executive Board.

President Toomey: The report of the Treasurer is next.

Dr. Grulee: I am going to ask Dr. Martmer to explain several features of the report, since he is Chairman of the Budget Committee.

Dr. Martmer: At first glance, the Treasurer's report looks as though the Academy is an extremely wealthy organization. However, there are certain facts which must be kept in mind. As of this moment, we have cash in the bank totaling $129,767.89. But remember that the Treasurer of the Academy is custodian of those funds which are furnished by the various commercial firms for the ICH Committee, and there is definitely blocked for the ICH Committee—since they have collected that amount—$40,255.00, which leaves us, then, a balance of $89,512.89, which is actually Academy funds. At the start of the year, we had a balance of $43,859.98, and therefore, without going into our reserve, we have available for the balance of the year the sum of $45,652.91.

We have, to offset that, eight months of the Academy year. An estimate of probable costs over that period is as follows: This Atlantic City meeting will cost us approximately $25,000.00. The cost of the Executive Board meeting for this session amounts to about $3,000 and there is a second Executive Board meeting in June, which will cost an additional $3,000. There are, in connection with the Areal Meetings, unpaid expenses which we have estimated perhaps somewhat high, but nevertheless a sum must be set aside for that purpose, and we have estimated $3,000. The office salaries, including the five people who are employed in the office, the Secretary and Assistant Secretary for the eight month period amount to $22,500. There is an item of $100 or more which we are obligated to pay in the furnishing of certificates for new members. We have committee expenses to the sum of $3,000 which was set up in the original budget, and of which a very small portion has been utilized up to the present, as Committee Chairmen have a habit of sending in their expense accounts about the 30th of June if not on the 2nd or 3rd of July of the following fiscal year. That amounts to $3,000.

Our telephone and telegraph expense amounts to about $500, based upon the first four months' experience. The rent for the offices is $1800, and there was allocated at the beginning of the year the sum of $600 to pay for postage and stenographic service on the part of the members of the Executive Board, State Chairmen, and others who have to deal with Academy correspondence. We have paid for that at the rate of 5¢ a letter plus the 3¢ postage, and of that sum $100 has been utilized up to the present in expense accounts rendered, so that there remains $500. Totaling those sums you have estimated expenses for the remaining eight months of $62,400.00. That looks very definitely as if we are going into the red. To offset that, we have registration fees paid at this meeting, and it is estimated that we will close the year with a slight rise above last year. At least that is the hope of the Budget Committee, because for the past seven years the Academy each year has progressively gone in the red to the extent of about $3,000 a year. In other words, seven years ago we had about $75,000.00 in the Treasury at the end of the year as opposed to the $43,859.00 that we had at the beginning of this fiscal year. It is our hope that the Academy will eventually be able to recoup its losses to the point where there will be maintained on hand a sum equal to approximately one year's expenses. The reason is, that if we had not had that $75,000 on

hand at the time that some of these committees started to function, it would not have been possible for us to advance the money to enable them to carry on some of the things that have been done.

President Toomey: New members.

Dr. Grulee: The following have been elected to fellowship: District I—Euclide Dóchene, Quebec; Charles Hilliard Hollis, Lawrence, Kan.; Ella Langer, Augusta, Me.; R. William Provenzano, Boston, Mass.; Gabriel J. Rubin, Boston, Mass.; and Thomas B. Walker, Portsmouth, N.H. District II—Margaret Dann, New York, N.Y.; Anne Drislane, Albany, N.Y.; John Edward Franklin, New York, N.Y.; Abraham Gilner, Brooklyn, N.Y.; Leon Greenspan, Bronx, N.Y.; James Quintin Haralambie, Larchmont, N.Y.; B. Winston Jarvis, New York, N.Y.; Benjamin Kaufman, Brooklyn, N.Y.; Maurice Kaufmann, Hempstead, N.Y.; Alexander S. Manne, Brooklyn, N.Y.; Charles William Neuhardt, West Bronxville, N.Y.; and William Owens, Brooklyn, N.Y.

District III—Abraham Berkow, Hackensack, N.J.; Ruth V. Berney, Newark, N.J.; Sydney H. Gurian, Newark; Joseph A. Hesch, Philadelphia; Thomas T. Kochenderfer, Norristown, Pa.; Marion McIlveen, Ridgewood, N.J.; Charles Rosenfeld, Philadelphia; Hubert A. Royster, Jr., Bryn Mawr, Pa.; and Ralph A. Warwick, Camden, N.J. District IV—Susan Coons Dees, Durham, N.C.; Albert Merritt Edmonds, Richmond, Va.; John R. Harvin, Sumter, S.C.; William R. Jones, Columbus, Ga.; Edwin Lawrence Kendig, Jr., Richmond, Va.; and Ethel MacMadden, Columbia, S.C. District V—Sandford F. Goodchild, Toronto; George Michie Laning, Detroit; Harry Braham Leslie, Cleveland; Albert L. Lewin, Euclid, Ohio; Robert J. Mason, Birmingham, Mich.; Ross Munro Matthews, Peterborough, Ontario; and Earl E. Smith, Cleveland.

District VI—H. Bruce Chown, Winnipeg; J. R. Goran, Moline, Ill.; Sydney Israels, Winnipeg; J. Howard Laubscher, Rockford, Ill.; Edwin F. Merolla, Waukegan, Ill.; Theodore C. Papermaster, St. Louis Park, Minn.; Marlin H. Poindexter, Jr., Fargo, N.D.; Raymond R. Rembolt, Iowa City, Iowa; Joe M. Standefer, Des Moines. District VII—Raymond B. Anderson, Kansas City, Mo.; Robert A. Gardner, Houston; John Paul Gibson, Abilene, Tex.; Roswell Johnson, New Orleans; John T. Kometani, New Orleans; Hugh W. S. Powers, Jr., Dallas; John Ray Powers, Baton Rouge; Henry B. Strenge, Oklahoma City; and B. H. Williams, Temple, Tex. District VIII—E. Johnston Curtis, Vancouver, British Columbia; Herbert Burroughs Ellis, Jr., Santa Fe, N.M.; Arthur M. Grossman, Los Angeles; William Caldwell Layton, San Mateo, Calif.; John William Schonwald, Oakland, Calif.; Carol Kander Smith, Santa Fe, N.M.; and Alvin DuBois Wert, Portland, Ore.

District IX—Nestor Salinas Aramayo, Sanchez Lima No. 1242, La Paz, Bolivia; Almir Madeira, rua Presidente Pedreira, 11, Niteroi, Rio de Janeiro, Brazil; Mauricio Martins da Silva, Av. Atlantica 762, apto. 1202, Rio de Janeiro, Brazil; Guillermo Morales Beltrami, Belbao 1933, Cas. 3620, Santiago, Chile; Emilio Aleman, Augustina 218, Vibora, Habana, Cuba; Juan Llort E., 7a Calle Poniente #13, San Salvador, El Salvador; Carlos Perez Cotera, Calle Arce 140, San Salvador, El Salvador; Alfonso Jimenez Castillo, 6 C. O. #4-B, San Salvador, El Salvador; Maria Isabel Escobar, 6 C. P. 59, Guatemala, Guatemala; Neri Flores Rodas, 13 Calle P. #51, Guatemala, Guatemala; Manual A. Giron, Callejon Normal #19, Guatemala, Guatemala; Carlos Lara Gonzalez, Cuarta Avenida Sur No. 25, Guatemala, Guatemala; Carlos M. Monson, 10a C.P. prol. #17, Guatemala, Guatemala; Alberto Vassaux Mendez, Callejon Concordia 48, Guatemala, Guatemala; Ruben Gorlero Bacigalupi, Av. Joaquin Suarez 2935, Montevideo, Uruguay; and Eugenia S. Yannuzzi de Lassabe, Pedro Olmida 2707, Montevideo, Uruguay.

Emeritus fellowship was granted to the following: Isaac A. Abt, Chicago; Floyd Clarke, Omaha; Bernard S. Denzer, Shelton, Conn. (formerly of New York City); William Weston, Columbia, S.C.; and Ernest Caulfield, Hartford, Conn.

The following resignations were accepted: Jesse R. Gerstley, Santa Fe, N.M. (formerly of Chicago); Arthur H. Hurd, Pasadena, Calif.; and George E. Oosterhous, Madison, Wis.

Dr. David Greene of New York, N.Y. was reinstated. Dr. William Langford of New York, N.Y. was elected to Associate fellowship.

You all know that we have developed sections in the Academy, and one of them is the Section on Surgery. The following have been elected Affiliate Fellows in that section: Alexander Harvey Bill, Jr., Seattle; Tague C. Chisholm, Minneapolis; Franc Douglas Ingraham, Boston; C. Everett Koop, Philadelphia; Willis J. Potts, Chicago; Henry Swan, Denver; Orvar Swenson, Boston; Oswald S. Wyatt, Minneapolis; Robert E. Gross, Boston; Donald Wieting MacCollum, Newton Highlands, Mass.; Frederick Robert Wilkinson, Toronto; Felipe Casho F., Hospital Infantile, Mexico City, Mexico; and Carlos Sarinana Natera, Nazas 16-A, Mexico City, Mexico.

President Toomey: The report was accepted. Now we come to the Committee Reports. The first will be by Dr. Coe.

Dr. Herbert E. Coe: Mr. President, The development of the Section on Surgery is a logical part of the present rapid expansion of the activities of the Academy. Surgical conditions have been discussed before this Academy in various ways for several years—Panel Discussions, Round Table Discussions, Symposia, etc., and usually by surgeons who have been invited for the occasion. These men have come and gone, they have presented their subjects, they have given us something worthwhile, and we feel that they were pleased to be here and present these subjects to us. However, they have had no integral part in the Academy, and they have had no particular interest in Academy work. A few of them have been elected to associate membership. For many years those of us who have been interested in the development of the surgery of infants and children have felt that there is a lack of a place of meeting. No organization to which we could come and where there would be a common interest, language and aims. I may say, personally, that in going to surgical meetings, the subject of children's surgery has received very scant attention. We would start to discuss something of surgical importance, perhaps malrotation of the intestines, which is highly important to all of us in the matter of treatment for infants, and neonatal surgical emergencies—they would listen politely for a few minutes, and say, "Oh, yes," ". . . I saw a case of that once, but the last 200 cases I had of carcinoma of the uterus I did so and so and so." And then we would gradually get them back to the subject of something concerning infants and children, and they would say, "Oh, yes. That's an infant; and when I took out the last 200 gall bladders, I did this and that and the other thing." The result was that we have had practically no chance to discuss problems which are of such absorbing interest to us. We have tried a number of times to have this matter brought up. We presented it formally to the Executive Board of the Academy at the meeting in Detroit. There it was considered very carefully by the Board. It was discussed again at the Pittsburgh meeting, and a committee was appointed at that time consisting of Dr. Paul Beaven, Dr. Bret Ratner and myself to study the situation and to consider enlarging the membership of the Academy to include those in allied branches of medicine whose work is limited to children. It seemed to us that it was a very logical development to go along with the purpose of the Academy of better care for children everywhere.—Not simply the care of children for medical conditions, but care for all conditions. The Executive Board made its report at the meeting in Dallas, and it was approved by the general membership. We went ahead with the formation of a surgical section, studying this field very thoroughly, planning who would be interested in this work and who might be logical members for the Academy. We made a report to the Board at its Milwaukee meeting last June. The Board then took the necessary steps that had been authorized at the Dallas meeting and formed these three sections. The Section on Surgery is now an integral part of the Academy. The men in that section, whose names you have just heard, feel a close interest in the Academy. At the meeting we held last night, it was very evident that they are not outsiders, that they are fellows with us. There is not a single surgeon on the program who has a detached interest. In that meeting we were assured the closest possible cooperation by Dr. Martmer in the formation of programs that he may use the surgical talent in supplying information of surgical aspects of any subject, whether Panel, Round Table or whatever it may be. Also, we hope that there will be surgical presentations before the entire Academy. We have also brought it out very definitely that the surgeons should be very careful not to go into too great detail in matters which are of interest primarily to the technical performances of surgery, but more in the idea of preoperative diagnosis and care, the preparation of the patient before operation, postoperative care and so on, matters which are of particular interest to anyone following the case.

With the development of children's surgery through this Academy, we can give better care to children everywhere, and the care of children in surgical matters will reach a higher plane. Let me just say in closing, that the role of a children's surgeon in a community right now is difficult. In many instances a children's surgeon is not received by a surgical college. Some surgeons feel that taking children's surgery out of their hands is splitting surgery up into many little pieces, and they oppose it in many instances. When a man comes into your community, whether he is limiting his surgery to children entirely, or whether he has a particular interest in the surgery of infants and children, please accept him and bring him into the pediatric group. The place of the pediatric surgeon in a community is with pediatricians, primarily, rather than wth the surgeons.

President Toomey: The next business is the Report of the ICH Committee.

Dr. Joseph Palma—Honolulu: Mr. President, members of the American Academy of Pediatrics, I move that the report of the ICH Committee as circularized to the membership be accepted with the following exceptions: that the statement on the bottom of page four and the top of page five headed, "Present status of recommendations for federal support of pediatric education," be deleted, and the following resolution substituted: "That, whereas, the Committee for Improvement of Child Health, in its reports to and with the approval of the Executive Board, has emphasized the critical financial situation of medical schools in general; and, as a result of the Study of Child Health Services, the paucity of resources available for adequate instruction in pediatrics, in particular;

And, whereas, largely through the initiative of the Academy interest in this precarious situation in medical education has been awakened among other groups including the AMA, the American Association of Medical Colleges, and even the federal government itself;

And, whereas, the Executive Board of the Academy in recent session, after due consideration of the efforts of general medicine now being undertaken to rectify the condition above noted, has adopted a resolution: "that the President of the Academy be empowered to appoint a Committee to work with a Committee from the AMA, if it was found that such a Committee was necessary."

Be it resolved that the American Academy of Pediatrics will not directly or indirectly seek federal aid to assist medical schools, not to support the specific discipline of pediatric education, but will await the approval of general medicine and medical education of this principle, at the same time offering every aid including its Study materials to the AMA and to others toward a solution of this important problem.

Dr. James L. Wilson: I should like to say a few words about the written report which you have. We had considerable discussion as to how long and how short it should be, and I would urge you to read it. It was a compromise, and compromises are apt to be ineffective. I want to emphasize that the really important thing in the Report is what we propose to do with the full time staff that we have acquired and with the relatively large sum of money that we raised in the name of the Academy, what we propose to do during this next year, and that the Academy now is undertaking to give its support to a charitable agency, for which we felt justified, in appealing for funds. We propose to place a great deal of emphasis in this next year on aid to education, undergraduate and graduate education, the latter particularly for an extension of education from out of the major centers of medical schools—the so-called decentralized teaching program. The proposal to delete the section referring to our appeal for federal aid is not important to the Committee, although I haven't quite digested it. The Report is a factual accounting of what was done. I personally regret that our Committee has been ineffective in informing the membership month by month of what we were doing and proposed to do. That was an error. The action of the AMA referred to is an admirable one, for which we in this Academy can take great credit. If the action to raise funds from private resources in the huge amounts necessary is effective there will be, obviously, no need for the government to appropriate any money. I would call to your attention, however, the great likelihood that such action will be a failure, and the great likelihood that federal support, or rather I should say an extension of federal support from its present status relative to pediatric education, will be made. Now the thing that concerned the ICH Committee was the way that support would be given, as well as the fact. And I think it greatly concerns our Committee and its future activities to have a directive from you whether you want this Academy to be in a position to influence the way any future extension of federal support to education will be carried out, and I should well imagine that that involves many policies which you need to settle once and for all.

Is this Academy going to try to influence legislation enough? As I remember it, the whole job of doing the survey was undertaken with the idea of making this Academy an effective instrument in influencing not only legislation, but what is done by other groups in positions in regard to child health. And it is a basic policy which you need to settle. We have got to have it settled before we can go further raising private funds for the staff of the ICH Committee to carry on its activities. We've got to have it clear what you want us to do.

Another word about the overlapping of committees. Confusion was inevitable when the ICH Committee was proposed, and it has taken us some time to iron out the confusion, and we haven't finished yet. You may see an example of how we propose to iron it out, however, in our action toward aiding education, with the instruments which we have at hand. This has nothing to do with federal aid right now. In this respect, we are overlapping the Committee on Education. The

function of the staff of the ICH Committee was to find not only how to serve the ICH Committee as such, but any other committee within the limitations of our financial resources. So here is an example, where the major part of the activities of the ICH Committee is to aid the Committee on Education, with their approval and at their request, and there is no reason why this shouldn't take place in regard to other committees. I realize how many controversial points there are to come up. But it is essential for our Committee to have the Academy define its general principles again, that had already been accepted at the time you undertook to do the Study, so that we can go ahead and honestly approach the private foundations, etc., from whom we have received funds.

Question from the floor: Are we discussing the motion to accept the entire report, or the motion to make a substitution in the report?

President Toomey: We are discussing the motion to accept the report, including the resolution offered.

Dr. Park J. White—St. Louis: These two things should be made subjects for separate consideration, because it might lead to rejection of the report on the basis of this one controversial subject. If we don't follow up the work and the results of our Study in such a way that the Academy can take the leadership in future developments, our efforts will have been wasted. I suggest we separate these two things one from the other.

Dr. Palma: I suggest, as I phrased the motion, the deletion of the two paragraphs in the Report and the substitution for those two paragraphs of a resolution. If you vote down the motion as stated, there is nothing to prevent anyone from moving the adoption of the report as published and presented.

Now, I would like to clarify the stand that I have taken. As a matter of principle, I am opposed to any further efforts to socialize this nation. We are already too far along the road. For reasons which should be clear to everyone, as you read your history, the end result of socialism is a police state. If that is what people want, it is what they will get, but I want my privilege of resisting up to the point of getting shot, which is the end result of a police state. More than that, pediatricians and those we are also intimately connected with medical colleges and other medical activities have asked, and in some instances directed, that the Academy not take the lead in a further experiment in socialization of this country. It will result in the destruction of the medical system as we now know it, which is pretty good, and which has been productive of one of the finest medical systems in the world. I represent those men who are in the middle and on the right and not on the left, who say that we should make a definite stand for or against this issue. They want to know where the Academy stands without equivocation. It is possible that members of the Academy will be asked to chose, at the county level, between their membership in organized medicine and membership in the Academy. I am fundamentally and unalterably opposed to any device, no matter how high sounding, to extend socialization. It will not result in improved health, it will not result in better education, it will not result in better medical schools. It will help result in a police state. I will have none of it.

President Toomey: Dr. Butler, I thought I saw you raise your hand.

Dr. Allan M. Butler—Boston: I move that we amend the amendment that has been proposed to the ICH Committee's Report. I would like to make this amendment in the interests of conservatism, that instead of giving a blanket deferment of action by the Academy, on this problem of adequately financing medical care, that we substitute a phrase: "the Academy will postpone, for a short period of time, action and will observe the results of the AMA's attempt to meet this need by raising money through private sources. I would like to stress why I do this in the interest of conservatism. Dr. Fishbein spoke in Boston on Tuesday a week ago. It was the impression of those who heard him that the AMA, if it failed in its attempt to raise the money adequate to finance medical education across the entire board, would then endorse the federal subsidy of medical education. There are some of us who are conservative enough, who have struggled for some time to learn how the federal government can step into medicine without being forced to do so—over the whole board of either medical care or service at one time. The solution of that problem is difficult. It can be accomplished by confining action to children, pertaining either to education or service. Without discriminating against any section of the people, you can limit action to children and you can give a clear definition of your limitations. Everyone is interested in children. All of us have passed through childhood and what we are has in a little extent depended on the medical care we had as children. Therefore, I suggest that the ICH Committee has not

with careless thought cited the initial step that may have to be taken to support medical education—it should be taken over this clearly defined, limited area, so that we are not confronted with the radical business of trying to finance all medical care by federal support before we have had some experience over a smaller problem.

President Toomey: There are now before the house an original motion, and the amendment.

Dr. Clifford Sweet—Oakland, Calif.: The paragraph which Dr. Palma wants to delete is as follows: "Subsequent to this Committee's recommendation for federal support of pediatric education, approved by the Executive Board on February 8 and again on April 30, 1948, the AMA has initiated plans to attempt to raise from private sources a large fund annually for medical education. Consequently on June 26, 1948 the ICH Committee recommended to the Executive Board that action to seek federal aid be held in abeyance without prejudice to justification of federal aid or its need. This recommendation was approved. The Committee also recommended that this plan of the American Medical Association to raise funds for medical education be supported by the Academy." I see no reason whatever for Dr. Palma's resolution. It says right here we will hold it in abeyance pending the action of the AMA. Dr. Palma's resolution should be defeated decisively.

Dr. Borden S. Veeder—St. Louis: My interest is in medical education, and medical education is at a crisis. I say that because I have been in pretty close touch with it now for the last six or seven year as the pediatric representative on the National Board of Medical Examiners, which has put me into close contact with teachers and the deans of medical schools and the work they are doing. I stand, perhaps, in the middle of the road, in the sense, politically, in believing in the rights of the individual. I don't like the right which tries to tell us what we shall not do, and I don't like the left which tells us what we must do. There is a middle ground somewhere. As a matter of fact, what has been interjected into this discussion of medical education is one of political philosophy that does not belong in our discussion. We ought to discuss it purely and simply from the standpoint of medical education. There is no question that schools and all of us who are dependent on education in the medical school are in bad shape financially. How to continue medical education on the basis that we have it now and have known it in the past—what the solution is I am not big enough or wise enough to know. I think no one knows. Our Academy Committee did a wonderful job in bringing up the point of the importance of medical education and particularly of pediatric education. It stirred into action the motion about which a great many were talking, and very few were doing much about. It has been leadership of that type that this Academy has had over the last 17 years. It has made the Academy what it is today. I am not a proponent of federal education or federal support; certainly we question very much its value, unless we can be adequately assured that there will not be federal domination. That probably might be possible. But this action of pointing out and urging and asking for federal funds was a good thing. After all, it isn't just a question of pediatric education. It is medical education in general. It is a much bigger field than just pediatrics, but all that we pediatricians are qualified to speak upon is the question of pediatric education, and that is why we have a right to say something. That is why this Academy was founded 17 years ago, so that we pediatricians could speak about things that have to do with the health of children, and if it hadn't been for that there wouldn't have been any Academy. They have done a very wise thing with this general action of the AMA that came up—they were more or less goaded into it through the Committee of Medical Education by the Academy report—to go out and raise funds for medical education. That is fine, and I sincerley hope that sufficient funds can be raised for medical education. We ought to respect the action that was taken in June and it seems to me end it right there. We stand perfectly pat on the subject, hold ourselves in abeyance, make no direct action, no direct move at the present time to seek funds for pediatric education. If funds are raised, the issue is over. Every school would rather have its own funds from a general fund not backed by any tax fund. On the other hand, there are two things that will happen if we do not raise the funds. One of them we may have to go back to. We ought not to put ourselves in a position where we are opposed to it because of a political philosophy. Let's stick to the question of education and answer the question of what we do on the basis of education alone. Now it may also happen, gentlemen, that within this next year or two, while we are trying to raise funds, there will be legislation introduced, maybe even passed, for federal support of medical education. If this is so, we should be in a position, through our Executive Board and through our Committees of experts who are fully acquainted with this, to have very definite statements—be in a definite position to say how this should be used and how it should be controlled. If we adopt this

resolution of my friend, Joe Palma, our hands will be tied. We will do nothing directly and we will hold everything in abeyance until the whole medical profession is united. It is very much better to let the whole matter go in this report as it was originally presented. It simply means that the Academy as a group is not going ahead on propaganda or work to raise money or to get money from federal sources until such a time as it is shown that the outside attempts from private sources are successful or unsuccessful. For if, in the meantime, there is legislation introduced and passed, perhaps, for federal aid we certainly should be in a position to say how that money should be used so far as pediatrics is concerned. After all, our fundamental purpose is better medical care for the child, ad it is my sincere belief that better medical care for the child is dependent upon two things: first, the character of the physician, and second, his education. And it is not dependent on the method in which the doctor is paid. We can not have good medical care unless we have sound medical education in our schools.

Dr. Oliver L. Stringfield—Stamford, Conn.: If this motion is passed, it will negate the action of the Board in Milwaukee in June—that we would cooperate with the AMA and hold in abeyance any requests for federal aid. We must remember one thing: we are all for good medical care and we are all against the socialization of medicine. Last spring I discussed this problem with a member of the Board of Trustees of the AMA and three other leaders in the House of Delegates of the AMA in my state. After the meeting of the Board in Milwaukee, I immediately sent a copy of our resolutions to each of them, and each one approved the action of the Executive Board and commended us saying that they could not see anything at all wrong with it. I called their attention especially to the abeyance section, and they said, "All right, because if we can not raise funds from voluntary sources, we want to have the benefit of the Academy helping us, if we have to go to federal sources. Dr. Howard, who is President of the National Organization of Officers of the State Medical Societies has said he brought to the Executive Board recommendations for a resolution which was to the effect that the Academy establish liaison committee which would cooperate with a similar committee to be established by the AMA in furthering our viewpoint. At the Executive Board meeting last night Dr. Howard's suggestion was fulfilled and such a committee was authorized by the Executive Board. A similar committee has not yet been appointed by the AMA because they do not meet until next week.

Dr. John Glenn—Houston: There seems to be confusion about what we all mean. None of us want federal control of medicine, we don't want federal control of education, we don't want a police state—there are many things we don't want. The ICH Committee's recommendation was made by a very honest and sincere Executive Board who felt there would be no objection to it. That was done in February of this year under the section of the Constitution which says, "it shall be the duties and powers of the Executive Board to transact all business arising in the interim between the annual meetings of the Academy, and required to carry out the objects of the organization." In order to enforce further such duties, it was to transact all business, not otherwise provided for, that may pertain to the Academy. In spite of objections which came to the ICH recommendation, this matter has not come to a mail ballot which might have been taken after the crisis for which this hurried recommendation was made was past; and to the present day—perhaps it will come today—there has been no vote of the members of the Academy on this thing. In spite of the fact that I had no vote to say whether I liked it or didn't like it, I was represented to the general medical profession of Texas as being in favor of federal subsidation of medical education. This fine republic from which I come is made up of a group of rather independent feeling citizens, who are considering seriously the length of time it will be if things continue to go as they are going now before they will be on a subsistance level of living with some conoisseur saying who may go to medical school, when he finishes medical school where he shall practice, and at what salary. It is for this reason that it was brought up in the Executive Council of the State Medical Association that perhaps it would be well to ask the members of the Academy to make a choice between the Academy and their county medical societies. We explained that this thing had never come before an Academy meeting. That the thing was an action of aminority in the Academy, and that until such time as it could come up we felt that it would be only fair on their part if they would let us remain members of our county society, and the proposal was, therefore, at that time dropped.

There has been some wise discussion about what Dr. Palma's resolution has meant. It simply is this: this thing was passed as described. The AMA said, "We don't like it, but we think maybe

you boys have something on medical education and we will try to raise the funds." And now we go back to them and say, "All right. We'll wait a reasonable length of time, and if you don't get it, we're going to ask for federal funds." We're holding an axe over their heads. They think we are a minority and they're right in the medical profession; they wonder if we stand with them or against them, and without such a change as this, which would give them assurance that we not only will stand with them, but we're going to stand behind them and help them in their decision. If they come to a decision that federal funds are necessary for medical education, they'll say so—and that is what this amendment means: that we, in the Academy, will get off of federal aid and not mention it again or not say we will wait a reasonable length of time, but we are saying that when you decide that medical education must be subsidized federally, and there is a lot of difference between federal and state, when you are ready for that then we're with you.

Dr. Joseph Stokes, Jr.—Philadelphia: May I point out the fact that we have had unquestioned evidence that the AMA will back federal support of education if it is found impossible for them to obtain the necessary funds from private sources. We should forget this question of federalization. It has nothing really to do with the present problem, and it seems that we have been rather mixed up by the amendment that Dr. Butler made. I should like to ask him to withdraw his amendment. The motion we have before us completely ties our hands. We have full realization that the AMA through its Council on Medical Education will back federal support of medical education if they are unable to get funds through private sources. I should like to see this motion brought up without Dr. Butler's amendment so that we can vote upon it and turn it down.

Dr. Butler: Instead of acting on the amendment, I would rather act on the report of the ICH Committee. With my amendment to the amendment before the house, the first thing that has to be acted upon unless I withdraw my amendment to the amendment, is the motion as amended by my amendment. Instead of doing that, I would like to withdraw my amendment if Dr. Palma will withdraw his amendment, and permit us to vote on the report of the ICH Committee.

Dr. Palma: I made a motion and incorporated in that motion to accept the report, except for two paragraphs under a certain section for which a resolution would be substituted; so I have a motion before the house and not an amendment. I am not of a mind to withdraw my motion for reasons previously stated.

Dr. Warren R. Sisson—Boston: It has been my position to have started the Study, and to carry on through the ICH Committee and to have seen the thing from its genesis to the present situation. We are all working for the same thing as far as I can see; namely, to promote the health of children and to extend the boundaries of child health, increasing them and improving their quality. We have given this matter a great deal of thought, and we have tried not to let our emotions guide us, but to let our intellect and the facts lead us. We now have an administration which is undoubtedly going to carry out some form of federal supervision or federal subsidy to medicine. The writing is on the wall. It is not a question, gentlemen, of what we should not do; it is a question of what we should do and how we can help the present situation. Mr. Ewing and his group know entirely the facts in our Study and it is going to be acted upon. May I inform you that I have had the opportunity of meeting with the AMA, and in a measure have been successful in expressing to the AMA that we are very willing to work with them. Furthermore, I get the distinct impression that the AMA thinks just as the ICH Committee thinks.

Dr. Butler: I would like to permit voting as the Academy really wishes to vote. I would like to stick, however, to running the meeting according to the parliamentary rules of Roberts. Even if Dr. Palma's motion is a motion, not an amendment to the ICH report, there has now been made an amendment to Dr. Palma's motion. Dr. Palma's motion can't be voted on until the amendment is voted on, but I would gladly withdraw my amendment if the Academy would like very clearly and very promptly to vote on Dr. Palma's motion and then get on to the rest of this business; perhaps even to endorsing the ICH report. I withdraw my amendment.

Dr. Philip Barba—Philadelphia: In the first place, I don't see how we can amend a committee report. We can accept it or reject it. It must be acted upon as a report without the resolution. In the second place, Dr. Glenn has stated that he felt that this original resolution was the opinion of a minority in the Academy. I think that this has been a little misrepresented, because in a good many of the states action has been taken which would clearly indicate the support of this resolution. In Maryland the fellows passed the resolution and signed it recommending the adoption of this resolution and it was passed by the Board at the meeting in Milwaukee to hold in abeyance requests

for federal subsidy and to support the AMA's action. A similar resolution was passed in the State of Massachusetts, and in Pennsylvania a poll has been taken and, while the complete returns are not in, so far a decided majority has accepted the resolution as passed by the Board. Now I believe the report states that similar action has been taken. I feel we can not truthfully say such feeling represents a minority of the Academy.

President Toomey: We are to vote on the resolution of Dr. Palma.

Dr. Roger L. J. Kennedy—Rochester, Minn.: The original motion which was to approve the report of the ICH Committee with an amendment was out of order and should have been so designated by the Chair.

President Toomey: This Chair still holds it is valid. The resolution is now ready for a vote. All in favor of this resolution say, "Aye." Contrary minded, "No." Not carried.

Dr. James M. Baty—Brookline, Mass.: I move the acceptance of the report of the ICH Committee as mailed to each member of the Academy.

President Toomey: All in favor. Opposed. Carried.

Dr. Grulee: I would like to announce that we have in attendance at this meeting a total of 2147 which is some 700 more than we have ever had at any meeting previously; and of that number there are 1305 physicians of which 899 are members of the Academy.

President Toomey: Next order of business: reorganization.

Dr. Baty: After the meeting in Dallas last year when the State Chairmen recommended to the President that a Committee on Reorganization be appointed to study the by-laws and suggest changes therein, such a Committee was appointed composed of Dr. Joseph Palma of Hawaii, Dr. Frank H. Lancaster of Texas, Dr. Edward B. Shaw of California, Dr. Frank Van Schoick of Michigan, and myself as Chairman. Our suggestions to the Executive Board are in two categories: one, suggesting specific changes in the By-laws effecting organization in an effort to have members participation of greater effect than we feel it is at the moment. It is suggested that all state groups of the Academy be organized for business purposes; whether they also include scientific purposes or not we would leave to the local group. The local groups should be organized so that they may elect their officers and the state chairmen be elected representatives of their groups. Further, the district chairmen, who constitute the Executive Board, should be electd by the membership in thier own district, rather than by the membership of the Academy as a whole. These recommendations are published in the minutes of the Executive Board meeting. I move that the By-laws be changed in accordance with these recommendations which were approved by the Board as a whole.

President Toomey: The motion is carried.

Dr. Baty: The Committee on Organization discussed many other problems of organization that we felt could not be solved at the moment. The general principle we have in mind is that the Executive Board is as at present the central power in the Academy and runs all affairs for us. Everything has to clear through them. We have thought of having all business matters in one area under the Secretary-Treasurer, and then have research, study and health problems handled separately —away from the ordinary business function. Your Committee has no specific recommendations in this regard, but we do feel that this matter should be studied and explored further. Mr. President, I move the adoption of the report of the Committee on Reorganization.

President Toomey: The motion is carried.

Dr. Frank H. Lancaster—Houston: The Publication Committee first wants to place before you our attitude in regard to advertising criteria and this was brought about by reason of the fact that the AMA refused to allow us to display PEDIATRICS at its last meeting. The outcome of this was a statement from them that any journal carrying advertising not Council accepted would not be permitted to display. The JOURNAL OF PEDIATRICS, which carries advertising which was not Council approved and which was displayed at the AMA, but they were required to tear out of that journal all objectionable matter, and by way of subterfuge, the one book was displayed on the Board, and underneath the counter they had all the others complete. Our criteria and standards, if you will read them in our own journal, are as high in every way as those of the AMA. Some of the products we will advertise in PEDIATRICS will never go before the AMA Council for approval, therefore, we would have to go without those ads entirely. So we have adopted the policy of judging our own ads and not worrying about the display at the AMA.

Our subscription list has increased materially. The Committee has decided to increase rates on advertising. We have now approximately 50 advertisers. Last June we had a deficit in our report

to the Academy ending our first volume of six issues and at that time we discussed ways and means of either reducing our costs or of increasing our revenue. To reduce costs was impossible, since costs were increasing all the time; therefore, the only way that we could hope to get ourselves over on the proper side of the ledger would be through increasing our revenue. Since that time we have added quite considerably to our income on advertising. The present indication is that we will reduce the deficit to some extend and in all probability in another six months, since we have now more prospective advertisers, we will probably be in satisfactory financial condition.

Question from the floor: How much will the increase in rate be?

Dr. Lancaster: The amount to increase rates is now being considered. It will be based on the rise in our number of subscriptions—that is additional doctors the advertiser is reaching.

President Toomey: Report accepted.

Dr. Grulee: It is now my unfortunate duty to announce to you the deaths of the following since our June meeting: Dr. John Aikman, Rochester, N.Y.; Dr. Walter C. Bacon of Baltimore, Md.; Dr. Bert I. Beverly, Oak Park, Ill.; Dr. Alberto C. Gambirassi, Buenos Aires, Argentina; Dr. Lawrence C. Goldman, Clayton, Mo.; Dr. George Clifford King, Fall River, Mass.; and Dr. Abel Lax, Outremont, Quebec.

President Toomey: Will you all rise for a minute? I will now ask Dr. Richard M. Smith to read the obituary for Dr. Hamill.

Dr. Smith: American pediatrics lost one of its most inspiring leaders in the death of Samuel McC. Hamill on May 3, 1948. The record of his professional achievements is well known to the older physicians in this group, but it is probably less appreciated by those who entered medical practice in recent years. Dr. Hamill graduated in medicine from the University of Pennsylvania in 1888, president of his class. After two years of further studies, he began practice in Philadelphia. He taught in various capacities at the Medical School until 1920. He was Attending Pediatrician at St. Christopher's Hospital for Children, Chief of the Pediatric Department of the Howard Hospital, the Philadelphia Polyclinic Hospital and the Presbyterian Hospital. He was active in numerous medical societies: Chairman of the Section of Diseases of Children of the AMA, first Chairman of the Section of Pediatrics of the Medical Society of the state of Pennsylvania, President of the American Pediatric Society, founder of the American Academy of Pediatrics and its President in 1932-33. A more detailed statement of his activities is recorded elsewhere.

Dr. Hamill will be remembered primarily for his contribution to the field of child health. Beginning with the Society for the Study of Prevention of Infant Mortality through the Child Health Association, the establishment and development of he Children's Bureau, the White House Conference of 1930, the post-World War I expansion of child health interest, and the founding and growth of the Academy of Pediatrics. His influence was great. His guiding hand was manifest in policies and works. In his native city he served with distinction on most of the committees working for children. For all the years of his active life, no important endeavor for children occurred in this country in which he failed to take a leading role. Dr. Hamill stood for high ideals and unselfish devotion to the children of the world. He gathered around him many younger men, and inspired them to strive for the things which were best in child health activities. The publications which came from the medical section of the White House Conference of which he was Chairman are standard documents, still the basis for information and research. In 1933 at the age of 70, Dr. Hamill became Chairman of the Pennsylvania Emergency Child Health Committee. He considered the work of this Committee the most important opportunity of his life. Three years later the Medical Society of the State of Pennsylvania gave him the Award of Honor. In presenting this award the President said his service to the children of Pennsylvania proudly transcends the individual contribution of any other doctor in our time in this state. He received also the first Gold Medal of the Philadelphia Pediatric Society and the Stritmader Gold Medal from Pennsylvania County Medical Society. For over fifty years this great soul, through example and precept, led the forces working for the betterment of the lives of children. The Academy can honor his memory most fittingly by carrying on along the trail which he blazed.

President Toomey: We now come to resolutions which may be presented before the house.

Dr. Grulee: Be it resolved that the Academy expresses its sincere appreciation to the local members of the Atlantic City area, Drs. Walter B. Stewart, E. Harrison Nickman, and Martin Green, for their splendid cooperation in the planning and conduct of the Annual Meeting held at the Chalfonte-Haddon Hall, November 20-23, 1948.

Be it resolved that the Academy expresses its sincere appreciation to Dr. Tom Mitchell for his untiring efforts in arranging the scientific exhibits at this meeting.

Be it resolved that the Academy expresses its sincere appreciation to the management of the Chalfonte-Haddon Hall for the splendid cooperation of all the hotel executives as well as the employees, and especially to Mr. Joseph I. McDowell, General Manager, Mr. David Parris, Mr. Ellsworth Sooey, and Mr. George J. Turcote, during the entire period of the meeting.

Be it resolved that the Academy expresses its sincere appreciation to Mr. Allan Nolte, assistant to the Maitre d'hotel, for his cooperation during the meeting.

Be it resolved that the Academy expresses its sincere appreciation to the Atlantic City Convention Bureau for their assistance during this meeting.

Be it resolved that the Academy expresses its sincere appreciation to the Ladies Committee, the commercial advertisers (enumerated) and spcifically to the Kimball Glass Co. for publishing the Academy bulletin daily during the meeting.

Resolutions all carried.

Dr. Grulee: The following telegram has been received from the Philippines: "Greetings and best wishes to the officers and members of the American Academy of Pediatrics for a successful annual meeting," from Fay del Mondo.

The following resolution came from the meeting of the Executive Board and the State Chairmen and the Committee Chairmen: The most immediate prerequisite for medical care for children is more adequate training in pediatrics for all practitioners who care for children, and

Whereas, the recent Study of Child Health Services conducted by the American Academy of Pediatrics shows serious inadequacies in the financial support of the pediatric training in medical schools and almost no funds to develop teaching affiliations with outlying hospitals, and

Whereas, the Academy recognizes the need to substantially increase financial support of medical education as a whole, even though the Academy Study was restricted to problems affecting pediatrics, and

Whereas, the AMA has gone on record favoring an intensive effort to secure voluntary support for medical education, and

Whereas, the need for professional leadership of the program to improve medical care is so urgent that assumption of this leadership in the area of medical training must not be unduly delayed, therefore,

Be it resolved that this Academy is sympathetic with and will support the effort of the AMA to raise the necessary funds for medical education from private sources.

Be it further resolved, that if this private support is not attained within a reasonable length of time, the legislation to allocate federal funds for this purpose should be vigorously supported provided that such legislation contains specific safeguards to protect the freedom and initiative of physicians and of medical institutions.

President Toomey: Moved, seconded and carried. Any other resolutions? Dr. Hurtado.

Dr. Felix Hurtado—Havana: Members of the Academy, it is a great pleasure to present to you a cordial invitation to attend the second Pan-American Pediatric Congress, which will be held in Mexico City during November 2-5, 1949. At that Congress will be presented an interesting program on important subject matter to be discussed by speakers from Latin American countries and from the United States. All papers will be delivered simultaneously in English and in Spanish, with the kind cooperation of the International Machine Corporation. This meeting will be held in Mexico in the Hotel Prado. We hope that many fellows will be able to attend in order to maintain our many Latin American friendships.

President Toomey: Now we come to the report of the Nominating Committee.

Dr. William W. Belford—San Diego: Since we have amended our By-laws and changed the method of election of District Chairmen, I would move that the new changes in the By-laws be temporarily suspended until the conclusion of the election of officers for the coming year.

President Toomey: Carried.

Dr. Belford: In accordance with Article I, Section 8 of the By-laws the following report is submitted: Vice President (President Elect), Dr. Edward B. Shaw, San Francisco; District Chairmen: District II, Dr. Paul W. Beavin, Rochester, N.Y.; District V, Dr. Edward A. Wishropp, Grosse Pointe Farms, Mich.; District VIII, Dr. Crawford Bost, San Francisco.

President Toomey: Carried. . . . It is now my pleasant duty to install the new President, Dr. Warren Sisson.

Dr. Sisson: I merely wish to thank you for your vote of confidence and express to you my hope that during the next year we can carry on and fulfill the pleasures and obligations which this Academy has endeavored to endorse.

President Toomey: Meeting adjourned.

LIMITED